



Chest wall resections for sulcus superior tumors

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Abstract: Chemoradiotherapy followed by surgical resection (trimodality therapy) is a guideline recommended treatment for sulcus superior tumors (SST). By definition, SSTs invade the chest wall and therefore require en-bloc chest wall resection with the upper lung lobe or segments. The addition of a chest wall resection, potentially results in higher morbidity and mortality rates when compared to standard anatomical pulmonary resection. This, together with their anatomical location in the thoracic outlet, and varying grades of fibrosis and adhesions resulting from induction chemoradiotherapy in the operation field, make surgery challenging. Depending on the exact location of the tumor and extent to which it invades the surrounding structures, the preferred surgical approach may vary, e.g., anterior, posterolateral, hemi-clamshell, or combined approach; all with their own potential advantages and morbidities. Careful patient selection, adequate staging and discussion in a multidisciplinary tumor board in a center experienced in complex thoracic oncology leads to the best long-term survival outcomes with the least morbidity and mortality. Enhanced recovery guidelines are now available for thoracic surgery, promoting faster recovery and helping to minimize complications and morbidity, including infections and thoracotomy pain. Although minimally invasive surgery can enhance recovery and reduce chest wall morbidity, and is in widespread use in thoracic oncology, its use for SST has been limited. However, this is an evolving area and hybrid surgical approaches (including use of the robot) are being reported. Chest wall reconstruction is rarely necessary, but if so, the prosthetic materials are preferably radiolucent/non-scattering, rigid enough while still being somewhat flexible, and inert, providing structural support, allowing chest wall movement, and closing defects, while inciting a limited inflammatory response. New techniques such as 3D image reconstructions/volume rendering, 3D-printing, and virtual reality modules may help pre-operative planning and informed patient consent.

Keywords: Superior sulcus; Pancoast tumor; non-small cell lung cancer (NSCLC); chest wall; surgery

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Introduction

Background

Lung cancer is one of the most common types of cancer, and highly contributes to cancer-related mortality (1). Nearly 30% of patients with non-small cell lung cancer (NSCLC), which is the most common histological type of lung cancer, are diagnosed with locally advanced disease of which nearly 5% originate in the superior sulcus, also called Pancoast tumors. Treatment of such tumors is challenging due to their anatomical location, which is high in the apex of the lung (above the second rib), and due to invasion of the chest wall. More extensive tumors may also involve other structures, such as the brachial plexus, subclavian vessels and the spine, further complicating radical treatment.

Following two prospective multicenter trials which showed superior outcomes after induction chemoradiotherapy followed by resection (trimodality therapy) for patients with superior sulcus tumors (SST), this has become a guideline recommended treatment (2-5). Compared with chemoradiotherapy, this approach offers the possibility of better locoregional control, and more favorable overall survival in patients fit for surgery, even in patients diagnosed with tumors invading the spine or large vessels, those with limited mediastinal nodal involvement, or with low-volume (oligo) metastatic disease (6-8). Whether trimodality therapy is better than chemoradiotherapy followed by adjuvant immunotherapy is uncertain (9).

Rationale and knowledge gap

By definition, SSTs invade the chest wall, above the second rib. As a result, complete resection of the tumor requires pulmonary resection, *en-bloc* with a part of the thoracic wall. The addition of chest wall resection to anatomical pulmonary surgery, potentially results in higher morbidity and mortality when compared to a standard anatomical pulmonary resection (10). Chest wall resection may be challenging, as the thoracic outlet is a region of the body that is not easily reached, and where many important structures are located, such as the subclavian vessels, branches of the brachial plexus, phrenic nerve and stellate ganglion. Furthermore, extensive fibrosis resulting from preoperative chemoradiotherapy may further complicate resection in this area, and healing may be impaired. Intraoperative techniques vary depending on location of the tumor, and involvement of surrounding structures. Prevention of early and late morbidity is essential to

preserve optimal quality of life after such extensive surgery.

Objective

In this report, we aim to provide a concise overview of the surgical treatment of SST, with particular emphasis on the chest wall resection. Pre-operative planning and work-up, surgical techniques and prevention of morbidity, are discussed.

SST

Staging and pre-operative planning

For all patients with suspected NSCLC, adequate staging is mandatory. Currently, minimum guideline recommended staging for potentially resectable NSCLC includes histological diagnosis, a contrast enhanced computed tomography (CT) scan of the chest and upper abdomen and a “whole-body” 18F-fluorodeoxyglucose (¹⁸F-FDG) positron emission tomography (PET)/CT scan; invasive mediastinal lymph node evaluation with endobronchial ultrasound (EBUS), esophageal ultrasound (EUS) or (video) mediastinoscopy is indicated when suspicious nodes are present on imaging, or if the tumor is FDG-negative, centrally located or is larger than 3 centimeters (2). For patients with an SST, which is considered locally advanced disease, a magnetic resonance imaging (MRI) of the brain is indicated to rule out metastases before start of curative intent treatment (2). For most SSTs, a contrast enhanced CT scan gives optimal information on tumor size and local extent in the chest wall, e.g., the number and location of the involved ribs. A CT scan detects chest wall invasion with a sensitivity and specificity of 38–87% and 40–90%, respectively (11). Although this is a wide range, sensitivity increases with the presence of symptoms, such as pain and muscle atrophy on the ipsilateral side. The sensitivity for detecting chest wall invasion with MRI is 63–90%, and is comparable with CT, although specificity is more consistently, and is reported in the range of 84–86% (12,13). To determine vascular invasion, as well as the relationship of the tumor with the brachial plexus, an MRI is of additional value (14). Although CT scan is superior in identifying vertebral bony involvement in patients with an SST in close proximity to vertebral structures, an MRI may help to differentiate between reactive inflammatory changes and true vertebral invasion (15). Pulmonary function tests and cardiovascular evaluation before the start of treatment are

Table 1 Surgical and oncological outcomes for patients with superior sulcus tumors (studies including >40 patients)

First author	Year	Study type	Number of patients/resected	cT3/T4	Guideline recommended induction CRTx	Morbidity	Surgical mortality	R0	pCR/pCR ITT	Median OS (months)	5 yr OS	Prognostic for OS
Rusch (4)	2007	Prospective	110 (ITT)/88	78/32	100%	52%	2.3%	94%	36%/29%	33 (ITT)	44%	pCR (ITT)
Kunitoh (5)	2008	Prospective	76 (ITT)/57	56/20	100%	14% (major)	2.6%	89%	21%/16%	Not reached	56%	cT3, pCR (ITT)
Demir (16)	2009	Case series	65	55/10 (pT)	15%	26%	6.2%	82%	N/A	24	31%	Non-N2, R0
Collaud (17)	2014	Case series	65	N/A	80%	46%	6%	85%	29%	Not reached	69%	Response to induction, location, adjuvant treatment
Marulli (18)	2015	Case series	56	32/24	100%	11% (major)	5.4%	86%	18%	35	38%	cT3, R0, pCR
Waseda (19)	2017	Case series	46	18/28	100%	24%	0% (30-day)	96%	N/A (pCR + MPR 65%)	Not reached	63%	N0, pathological response
Ushida (20)	2019	Case series	60 (ITT)/54	46/8	100%	13% (major)	2% (90-day)	81%	22%/20%	Not reached	69%	pCR
Bertolaccini (21)	2023	Case series	100	N/A	9%	20% (major)	6.9%	85%	N/A	24.3	34%	N0, R0, posterior location
Ünal (8)	2023	Case series	123	76/47	100%	21% (major)	6.5% (90-day)	93%	42%	100	60%	MPR
Rzyman (22)	2023	Case series	48 (ITT)/47	N/A	100%	36%	2.1% (90-day)	89%	28%	Not reported	34%	Age <70 years, R0, tumor stage, pathological response

CRTx, chemoradiotherapy; R0, radical resection margin; pCR, pathological complete response; ITT, intention to treat population; OS, overall survival; yr, year; N/A, not available; N0, no nodal disease; MPR, major pathological response.

standard clinical practice (2).

According to the 8th edition of the TNM staging system for NSCLC, SSTs without distant metastases are staged IIB (T3N0), IIIA (T3N1, T4N0–1) or IIIB (T3N2 or T4N2). In general, patients with metastatic disease, especially those with multiple metastases, are not considered for surgery even though surgery may improve local control and potentially prevent debilitating pain due to brachial plexus or spine invasion. Resection in patients with limited mediastinal nodal involvement (N2) may be considered in carefully selected, fit patients, although outcomes compare unfavourably to those with N0–1 disease. Several other prognostic factors for improved survival have been identified (*Table 1*), e.g., radical resection (R0) and pathological complete response (pCR) to induction therapy (4,7,8,21).

After accurate staging, patients should be discussed in

a multidisciplinary tumor board, attended by surgeons experienced in complex thoracic oncological surgery (23). For patients with an SST invading surrounding structures, such as large vessels (subclavian artery or subclavian vein), or the spine, surgery may be especially challenging. However, in a recent series of 123 patients with SSTs, nearly 40% of which were T4 tumors (TNM 7th edition), extended resections were reported as feasible and safe, and resulted in high local control rates and good overall survival (8). Therefore, in the absence of a specialised team including vascular, orthopaedic, and neurosurgical expertise, patients should be referred to a center experienced with this type of extensive surgery; the trimodality approach, including surgery, probably offers the best chance of long-term disease control and survival (24).

Imaging techniques have improved over time, and recently, 3-dimensional reconstructions/volume rendering,

and virtual reality modules have been introduced to better visualise pulmonary anatomy, the primary tumor, and its local extension. These techniques may help to optimise pre-operative planning, and may facilitate informed patient consent before surgery (25). Although promising, the use of software to reconstruct 3D images is not widely used in clinical practice, partly due to a lack of experience by radiologists and other specialists (26). The use of 3D-printing in the preoperative planning for SST has not yet extensively been investigated, but might be of additional value in planning of complex, high-risk thoracic resections compared to conventional CT scans and MRI, and may even reduce operating room time (27,28). Although promising, this technique currently is only available in a few highly specialized thoracic centers.

Imaging is key in preoperative planning in thoracic surgery, e.g., to determine how many ribs are involved and the best surgical approach, but also to help with informing the patient about what to expect after surgery. For example, most SST tumors involve the T1-nerve root, which once resected, results in numbness of the ulnar side of the forearm. Sometimes, the stellate ganglion is involved in the tumor mass, and removal results in permanent ipsilateral myosis, and ptosis (Horner-syndrome). Vertebral resection and reconstruction frequently require the use of an osteosynthetic material, with a risk of hard-to-treat and persisting infection. Patients with a reconstruction of the subclavian artery with prosthetic material, need life-long antiplatelet therapy.

Surgical technique and prevention of morbidity

The standard surgical procedure for SSTs involves a pulmonary (anatomical) resection (e.g., lobectomy + mediastinal lymph node dissection) with *en-bloc* resection of the chest wall and involved adjacent structures. In case of poor pulmonary function, a wedge resection or (multi-) segmentectomy can be considered to preserve vital lung capacity. The preferred surgical approach strongly depends on the location of the tumor and involved structures, but also on the surgeons' preference.

Most commonly used approaches are the posterolateral (Shaw-Paulson), anterior [transmanubrial (Grunewald) or transclavicular (Dartevelle), and their modifications] and hemi-clamshell incision. Sometimes these approaches (posterolateral and anterior) are combined to gain adequate access to the thoracic outlet and important structures. The anterior approach may be preferred for patients with

vascular involvement because good vascular exposure can be obtained, but transection of the clavicle or manubrium is necessary to gain access, which introduces additional morbidity (29,30). The classic Shaw-Paulson thoracotomy, also known as the posterolateral approach, facilitates excellent exposure of the posterior chest wall and lateral part of the spine (31). It also offers good access to the nerve roots (C8, T1) and inferior trunk of the brachial plexus, and is the most appropriate incision through which to perform anatomical pulmonary resection and lymphadenectomy. The posterolateral incision also allows an intercostal muscle flap to be easily dissected from the ribs and fixed on the bronchial stump to reduce the risk of bronchopleural fistula formation. The hemi-clamshell incision, in which the lateral thoracotomy level may vary according to the size of the tumor, also gives excellent access to the anterior part of the mediastinum and great vessels (32). For patients with spinal involvement, a one-day procedure is possible, but we and others prefer a staged two-day approach, in which a dorsal approach for vertebral resection and posterolateral thoracotomy for chest wall and pulmonary resection performed on two consecutive days (33).

Minimally invasive surgical techniques are disseminating rapidly including for thoracic surgery. Video-assisted thoracic surgery (VATS) and robotic-assisted thoracic surgery (RATS) pulmonary resections are safe and feasible and have proved to result in comparable long-term survival and improved peri-operative outcomes when compared to an open approach in patients with NSCLC (34-38). Minimally invasive surgery, or a combined approach with open surgery (hybrid approach), is a technique that is increasingly being investigated for complex pulmonary oncological resections. Currently, there are case reports, but no robust evidence for its use in surgery for SST (39-41).

For tumors invading the chest wall, a complete (R0) resection contributes to improved survival, and the size of chest wall resection strongly correlates with postoperative morbidity. In most patients with SST, three or fewer ribs have to be partially removed to obtain radical surgical margins. For patients with posterior located tumors, this can be performed without the need for chest wall reconstruction. However, in patients with an anterior tumor invading larger parts of the chest wall, requiring three or more ribs to be removed, or more than four ribs for posterior tumors with risk of scapular impingement (*Figure 1*), restoration of the integrity of the chest wall is recommended to preserve chest wall stability, mechanics and respiratory function. This is in line with the recent

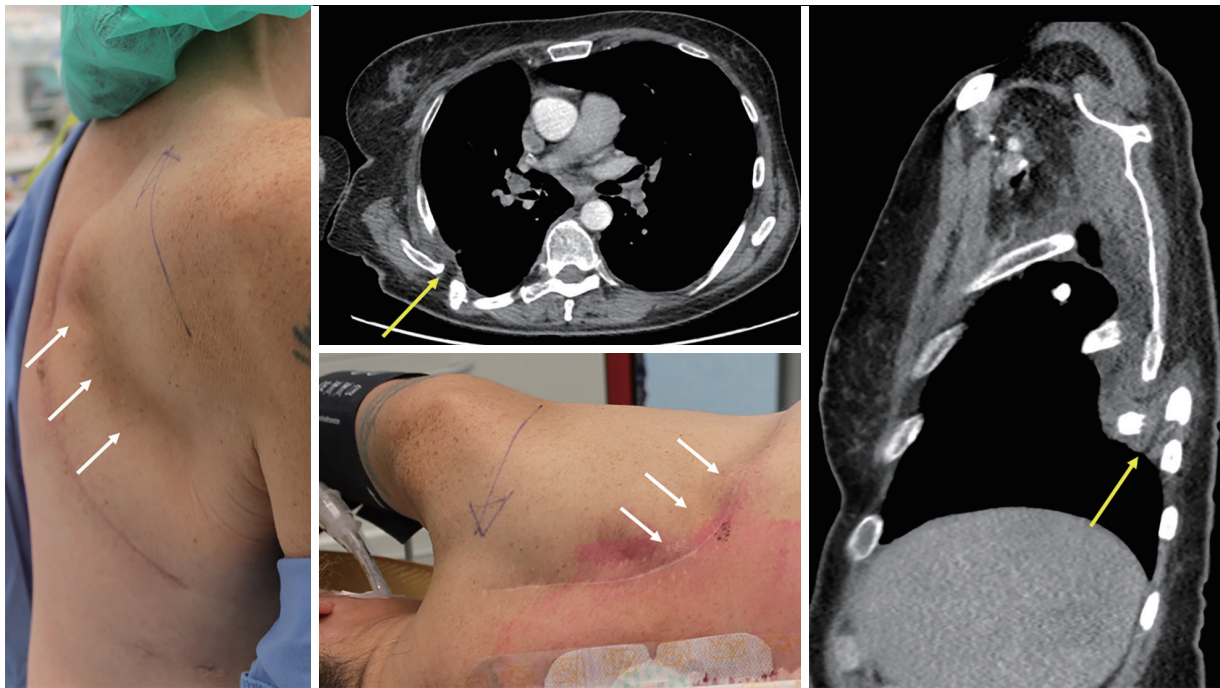


Figure 1 A patient treated with induction chemoradiotherapy and complete resection of a right-sided superior sulcus tumor: the right upper lobe, *en-bloc* with dorsolateral part of ribs 2–5, was resected, without primary reconstruction of the chest wall, which resulted in painful impingement of the scapula into the pleural cavity, which can be observed just above the incision line made to resect the superior sulcus tumor (white arrows), and destruction of the sixth rib (yellow arrows).

expert consensus on resection of chest wall tumors and chest wall reconstruction, in which rigid implants for chest wall reconstruction is recommended once the maximum diameter of the chest wall defect exceeds 5 centimeters (42). Patients with SST invading the spine represent a challenging group, especially for those whose tumor invades the vertebral corpus and spinal canal. Curative intent treatment with partial or complete, single or multilevel vertebrectomy, has been reported with considerable 5-year overall survival rates (43–61%), and acceptable and manageable morbidity in high volume, specialized centers (33,43).

For chest wall reconstruction, several materials are available. Preferably, the material is semi-rigid, i.e. stiff enough for structural integrity, but still flexible enough to allow chest wall movement, and inert, such that it induces a limited inflammatory response. In addition, the material should ideally be radiolucent or non-scattering to allow for detection of (loco)regional recurrences with conventional imaging techniques (CT or MRI) during follow-up. Although synthetic resorbable meshes are used [e.g., Vicryl (Ethicon, NJ, USA)], mostly to cover small

defects, we prefer the use of synthetic non-resorbable meshes for larger defects to obtain permanent stability [polytetrafluoroethylene (PTFE), polypropylene]. Their use is safe, allows for perfect sizing, and low infection rates are reported (<7%) (44). However, reconstruction can be difficult due to fibrotic tissue resulting from induction chemoradiotherapy, which may hamper proper fixation and ingrowth. Due to its location in the apex and removal of at least the first rib, solid fixation may further be complicated by the limited sites for insertion of the non-resorbable sutures. Rigid reconstruction with titanium ribs, biologic implants, or titanium meshes are rarely needed in patients with chest wall resection in the context of SST (45). With the use of synthetic meshes, a relatively high infection rate (6–22%) in chest wall reconstruction in non-contaminated defects is reported, with up to 42% requirement of removal of synthetic mesh (46). Therefore, biological meshes, or biosynthetic materials, in which biologic and synthetic components are combined, deserve consideration, in particular for patients at high risk for infection (47,48). 3D-printing techniques for reconstructive and restorative

Table 2 Bullet points

Guideline recommended treatment for patients with superior sulcus tumors is induction concurrent chemoradiotherapy followed by anatomical resection

Surgery for superior sulcus tumors is complex due to their anatomical location in the apex of the lung, adjacent to important structures such as brachial plexus, subclavian vessels and spine

3D-reconstruction techniques may help pre-operative planning and reduce operating room time

Reconstruction of the chest wall is rarely needed, but 3D-printing of patient tailored implants with biomaterial is a promising new technique

use, to replace resected structures such as chest wall or vascular structures with biomaterial, will facilitate surgery for complex thoracic tumors and overcome the disadvantages of synthetic material (26-28).

Impaired healing as a result from radiotherapy, extensive surgery and patient related factors, such as smoking history and diabetes, prompt aggressive perioperative measures to reduce the incidence of infection, e.g., antibiotic prophylaxis. Enhanced recovery programs are now available for thoracic surgery, promoting faster recovery and helping to minimize complications and morbidity, including infections and thoracotomy pain (49). With this approach, low morbidity and mortality can be achieved in patients with extended chest wall resections and reconstructions.

Conclusions

Table 2 summarizes key issues from this review. Trimodality therapy consisting of chemoradiotherapy followed by surgery is a guideline recommended treatment for patients with NSCLC originating from the superior sulcus. The optimal surgical approach depends on the exact location, extension to surrounding structures and surgeons' preference. Chest wall reconstruction is seldom indicated. All patients should be discussed in a multidisciplinary tumor board attended by thoracic surgeons experienced in complex thoracic surgery.

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