Current management of anterior Pancoast tumors

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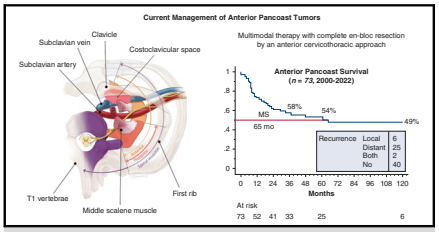
Video clip is available online.



Multimodal therapy with complete en bloc resection by an anterior cervicothoracic approach.

CENTRAL MESSAGE

In selected patients with anterior Pancoast tumors, surgery usually achieves R0 resection. With adjuvant and, in some cases, neoadjuvant therapy, 5-year survival was 54%.

Pancoast (or superior sulcus) tumors are non–small-cell lung cancers with direct spread to the apical chest wall.[1] They develop in the thoracic inlet, where commonly involved structures include the parietal pleura, upper ribs, proximal thoracic vertebral bodies, intervertebral foramina along the nerve roots, subclavian pedicle, phrenic nerve, lower brachial plexus roots, and stellate ganglion. Pancoast tumors account for <5% of all lung malignancies.[2] They raise difficult surgical challenges regarding selection of the best approach, achievement of complete en bloc resection to ensure local control, and reconstruction of resected structures to avoid functional disabilities. Major improvements in imaging have benefited the assessment of local and systemic tumor spread over the past 2 decades, allowing the development of surgical classifications and approaches that facilitate the surgical management.[3,4]

The aim of this study was to describe the current management of anterior Pancoast tumors at our institution, based on a new classification of Pancoast tumors that reflects our experience (IRB# Cerc-ctcv-2024-01-26_33230; January 26, 2024, with a waiver of consent). Outcomes are reported also.

CLASSIFICATION OF PANCOAST TUMORS USED AT OUR INSTITUTION

Pancoast tumors develop in the thoracic inlet, whose rigid boundaries consist of the manubrium anteriorly, first rib laterally, and first thoracic vertebra posteriorly. This small compartment contains the lung apex and major vessels and nerves. A major step in planning surgical treatment is selection of the approach that provides the best exposure for complete en bloc resection (R0) of the tumor and involved structures combined with extended lymph node dissection, while minimizing morbidity. To this end, we use a simplified classification into 3 categories: anterior, posterior, and spinal (Figure 1). The category is determined preoperatively based on computed tomography angiography (CTA) and magnetic resonance imaging findings.

Anterior tumors invade 1 or more structures anterior to the middle scalene muscle and spare the spine. The phrenic nerve, subclavian artery and vein, and brachial plexus are often involved, generating clinical symptoms. In contrast, due to the peripheral tumor location, symptoms related to lung involvement such as cough, hemoptysis, and dyspnea are uncommon initially. The anterior cervicothoracic approach is used to remove anterior tumors.[5] Close attention should be directed to the costoclavicular space delimited anteriorly and laterally by the medial third of the clavicle, costoclavicular ligament, subclavius muscle, and anterior arch of the first rib and posteriorly by the subclavian vein (Figures 1 and 2).

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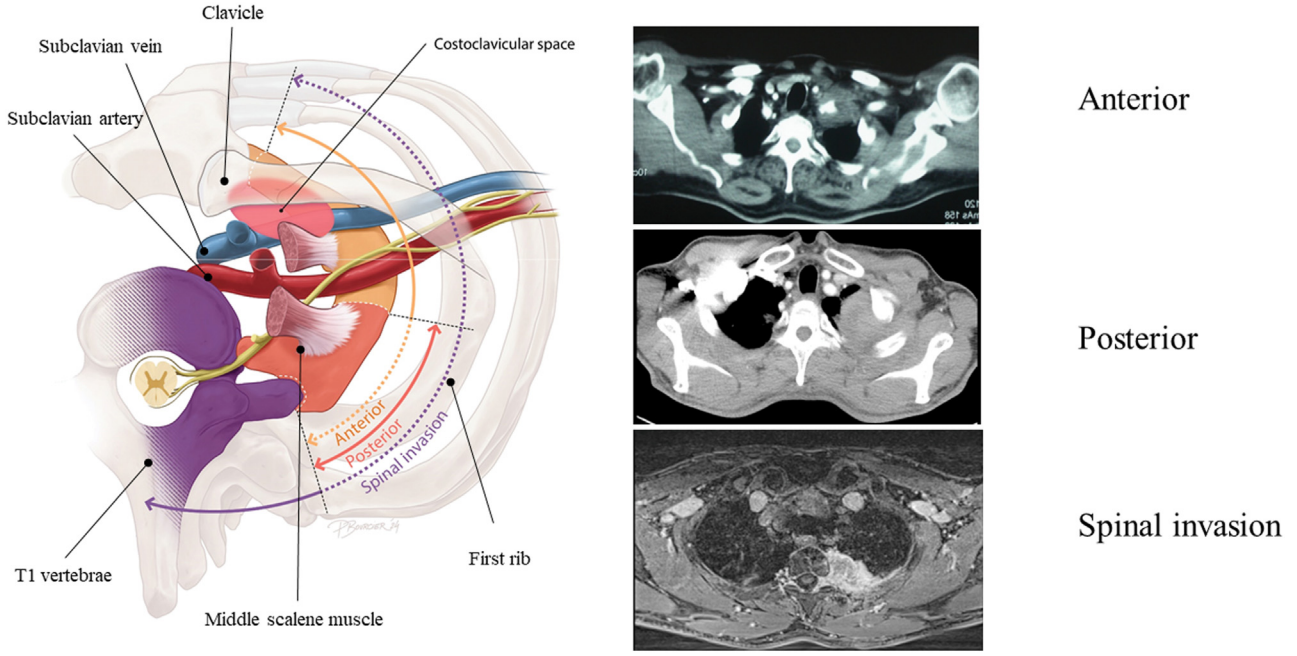


FIGURE 1. Anatomical classification of anterior Pancoast tumors with corresponding imaging findings. Anterior tumors (*yellow arrow*) invade 1 or more structures anterior to the middle scalene muscle and may extent posteriorly but spare the spine. Posterior tumors (*orange arrow*) are posterior to the middle scalene muscle and spare the spine. Spinal involvement tumors (*purple arrow*) are tumors invading the transverse process, vertebral body, and/or intervertebral foramina, regardless of anterior or posterior location.

Posterior tumors are posterior to the middle scalene muscle and spare the spine. Resection is through the standard Shaw-Paulson posterolateral thoracotomy.[4,6]

Spinal involvement is a separate category, regardless of anterior or posterior location. The transverse process, vertebral body, and/or intervertebral foramina may be invaded. The previously reported combined anterior and posterior midline approach is used.[7,8]

SURGICAL MANAGEMENT OF ANTERIOR PANCOAST TUMORS AT OUR INSTITUTION

Preoperative Workup and Patient Selection to Surgery

Routine tests include a standardized pulmonary and cardiac evaluation. Local tumor staging is by chest radiography; bronchoscopy; CTA and magnetic resonance imaging of the head, neck, and chest; and positron-emission tomography (PET). Vascular invasion is assessed by venous angiography, aortic arch arteriography, and duplex ultrasonography of the thoracic inlet. A biopsy is obtained preoperatively by bronchoscopy or percutaneously under CT guidance.

Endobronchial ultrasound replaced mediastinoscopy in 2010 for evaluating patients with mediastinal node enlargement by CTA and/or mediastinal uptake by PET. A supraclavicular biopsy is obtained when nodes are palpable in the neck.

Surgery should always be performed with curative intent. R0 resection is the main determinant of long-term survival. Consequently, surgery is not offered to patients whose preoperative workup findings argue against the feasibility of complete en bloc resection with R0 margins. Other contraindications to surgery sought during the preoperative workup are distant metastasis, invasion of the brachial plexus above the C8 root, invasion of the vertebral canal and spinal cord meninges, massive invasion of the scalene muscles and extrathoracic muscles, persistent N2/N3 disease despite induction therapy, and cardiopulmonary disease or other comorbidities of sufficient severity to jeopardize survival.

Anterior Cervicothoracic Approach for Anterior Pancoast Tumors

For the anterior cervicothoracic approach,[5] the patient is supine with the arms tucked and neck hyperextended and the head turned away from the involved side (Figure 3). A pad is placed under the shoulder on the involved side. The skin from the mastoid to the umbilicus and from the midaxillary line to the contralateral midclavicular line is prepped with a chlorhexidine-alcohol or povidone-iodine solution then draped with sterile sheets. The surgeon stands on involved side and the assistant on the uninvolved side. Care is taken to ensure sufficient space above the shoulder

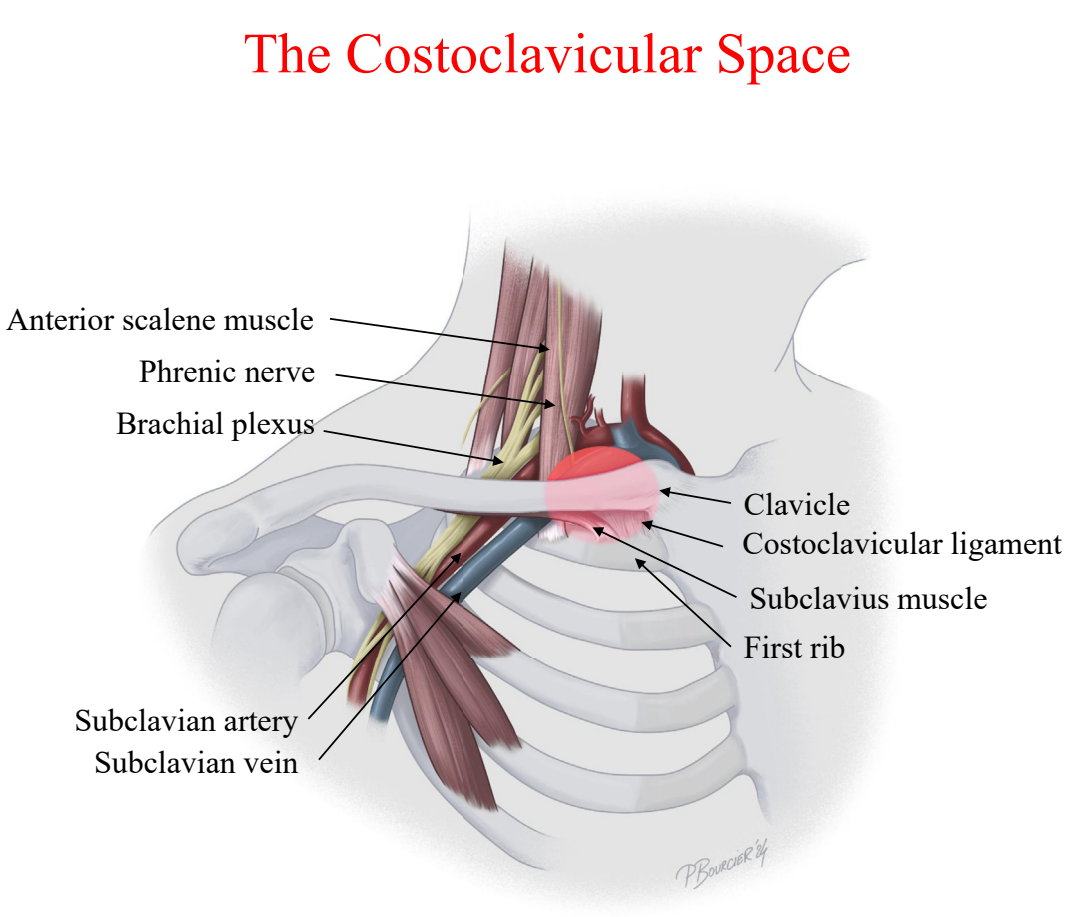


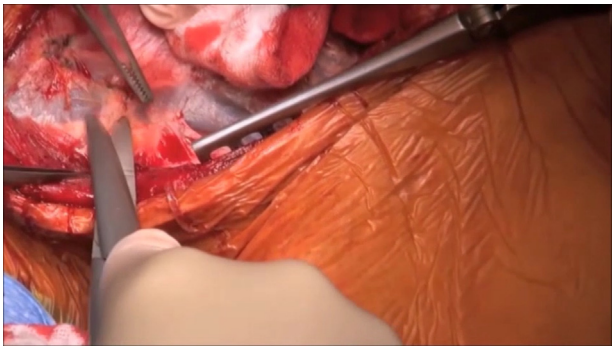
FIGURE 2. Diagram of the costoclavicular space.

and head of the patient for the surgeon to look down into the chest through the cervical incision. A bar is placed at the level of the hip to secure the chest retractor.

An *L*-shaped cervicothoracotomy is performed. The vertical component along the sternocleidomastoid muscle is carried horizontally below the clavicle to the deltopectoral groove. Resectability is then assessed. First, the scalene fat pad is dissected and assessed histologically for scalene node involvement (N3 disease). A frozen section analysis is routinely done to all suspect N3 lymph node and if positive the surgical procedure is stopped. After division of the sternothyroid and sternohyoid muscles, the surgeon runs a finger along the tracheoesophageal groove to assess the ipsilateral superior mediastinum. Tumor extension to the thoracic inlet is evaluated after opening the pleura through the horizontal incision, in a disease-free intercostal space. Evidence of pleural carcinosis is sought and gentle digital palpation is performed to confirm involvement of the lung apex (Video 1).

The next step depends on whether or not preoperative imaging demonstrated involvement of the costoclavicular space. If the space is involved, the transclavicular approach (Dartevelle approach[5]) is used. The sternal attachment of the sternocleidomastoid muscle is divided. The clavicular attachment is scraped off, together with the upper digitations of the ipsilateral pectoralis major muscle. A myocutaneous flap is then folded back, providing full exposure of the neck and cervicothoracic junction. The

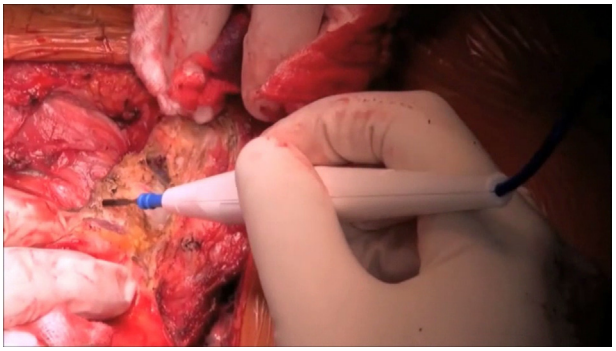
FIGURE 3. Patient position on the operating table.



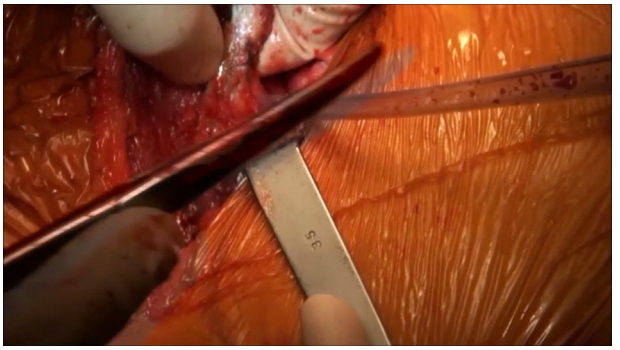
VIDEO 1. Evidence of pleural carcinosis is sought and gentle digital palpation is performed to confirm involvement of the lung apex. Video available at: https://www.jtcvs.org/article/S2666-2507(24)00156-1/fulltext.

clavicle is divided using a saw, the medial half of the clavicle is resected, and the sternoclavicular joint is cauterized (Video 2). If the costoclavicular space is not involved, the transmanubrial approach (Grunenwald approach[9]) is used. The superolateral portion of the manubrium (2 × 2 cm) is sectioned through an *L*-shaped incision to spare the sternoclavicular joint. The first costal cartilage is then divided under the clavicle with a disease-free margin. The internal thoracic artery is divided, allowing mobilization of an osteomuscular flap that is progressively elevated using a suture looped around the manubrial border allowing thus to have a large window to the cervicothoracic junction without dissection or mobilization of the distal clavicle (Video 3). Either for the transmanubrial or transclavicular approach, the pleural space is entered under the first, the second or the third rib in a disease-free area as previously assessed on the preoperative CTA. After cautious intrapleural digital palpation, all involved costal cartilages (from the first up to third cartilages if involved) are resected in a disease-free margin.

The jugular and subclavian veins are dissected then, once proximal and distal control is achieved, resected. These



VIDEO 2. The clavicle is divided using a saw, the medial half of the clavicle is resected, and the sternoclavicular joint is cauterized. Video available at: https://www.jtcvs.org/article/S2666-2507(24)00156-1/fulltext.

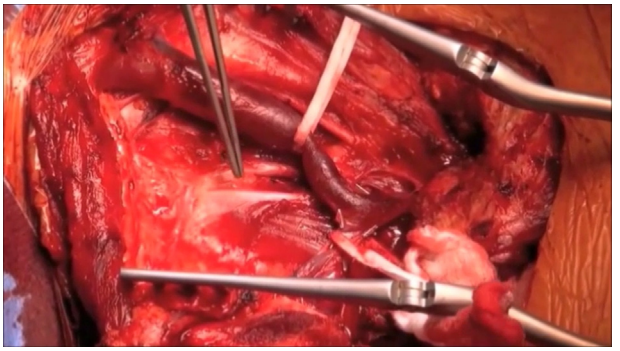


VIDEO 3. The internal thoracic artery is divided. Video available at: https://www.jtcvs.org/article/S2666-2507(24)00156-1/fulltext.

veins are not reconstructed if involved by the tumor. On the left side, ligation of the thoracic duct is usually required. Next, the anterior scalene muscle is divided with tumor-free margins. The phrenic nerve is carefully assessed and preserved if not involved (Video 4).

The subclavian artery is dissected and its involved branches divided. The vertebral artery is resected (and not reconstructed) only if invaded and in the absence of significant extracranial occlusive disease detected by the preoperative workup. If the tumor abuts the subclavian artery wall, a subadventitial plane is used to dissect the artery. If the subclavian, carotid, and/or innominate arterial wall is involved, the involved artery or arteries should be resected after achieving proximal and distal control, to ensure tumor-free margins. Arterial reconstruction is mandatory to avoid upper limb ischemia. End-to-end anastomosis can be performed if a tension-free suture is achievable. If not, a polytetrafluoroethylene graft (6 or 8 mm) can be implanted (Figure 4 and Video 5).

The middle scalene muscle is divided above its insertion on the first rib, with tumor-free margins. The C8 and T1 roots are easily identified and are dissected free in the out-to-in direction, to their junction forming the lower trunk of the brachial plexus. The ipsilateral prevertebral muscles,



VIDEO 4. The phrenic nerve is carefully assessed and preserved if not involved. Video available at: https://www.jtcvs.org/article/S2666-2507(24)00156-1/fulltext.

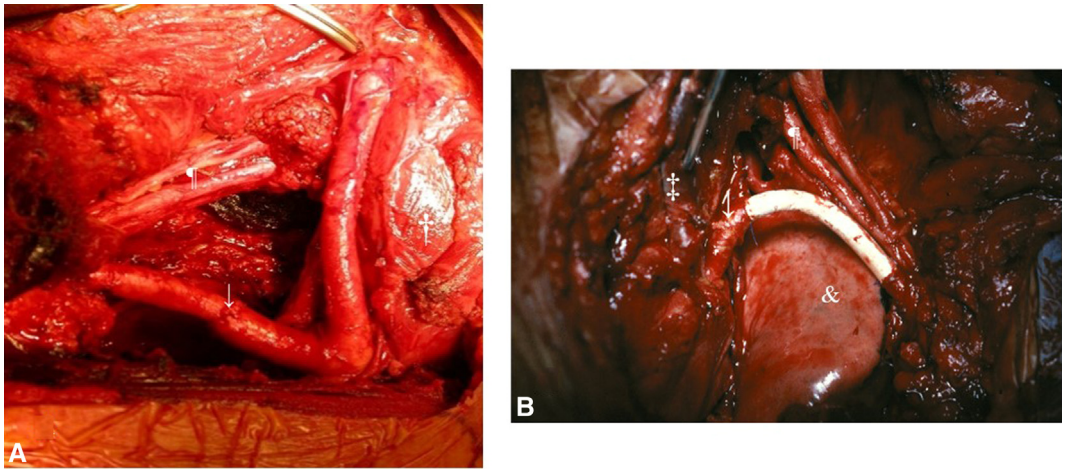


FIGURE 4. Subclavian artery reconstruction after anterior Pancoast tumor resection. A. End-to-end anastomosis. B, Polytetrafluoroethylene graft interposition. ¶Brachial plexus. ↓Subclavian artery. &Left lower lung. †Sternocleido muscle. ‡Internal jugular vein.

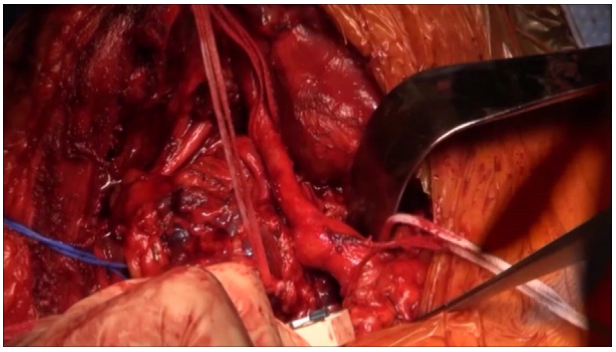
paravertebral sympathetic chain, and stellate ganglion are resected from the anterior surface of the C7 and T1 vertebral bodies. The C7-T1 intervertebral foramen is then clearly visible. The T1 root, if invaded, is divided distally at the junction with the C8 root and proximally beyond the presence of visible tumor, just lateral to the C7-T1 intervertebral foramen (Video 5). When the foramen is involved, the tumor is reclassified as involving the spine, left attached to the spine, and removed through the combined anterior and posterior midline approach.[8]

The chest wall resection is completed to the extent dictated by the spread of the tumor. Because frozen sections of bone are not feasible, the ribs should be resected at a wide distance from the tumor. The anterolateral arch of the involved ribs is divided at the costochondral junction. When necessary, the divided ribs are disarticulated from the transverse processes of the first 2 or 3 thoracic vertebras through the anterior approach. Upper lobectomy can be accomplished through this approach and followed by standard lymph node dissection, including stations 7 to 9 after opening the posterior mediastinum and pulmonary ligament (Video 6).

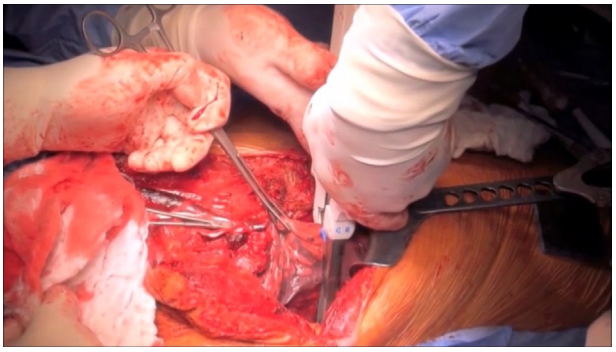
With the transclavicular approach, the sternocleidomastoid muscle must be inserted onto the sternum. With the transmanubrial approach, fixation of the manubrium is achieved using 3 separate steel wires, allowing complete stability of the clavicle. The cervical incision is closed in 2 layers. Conventional tube drainage of the involved side of the cavity is carried out.

MULTIMODAL TREATMENT FOR PANCOAST TUMORS AT OUR INSTITUTION

The technical demands raised by en bloc R0 resection of Pancoast tumors and the consequent high risk of local and/or systemic recurrence support multimodal treatment. Neoadjuvant chemoradiotherapy has provided good results, with the response predicting survival after surgery. However, Pancoast tumors are rare, contributing only about 5% of all lung malignancies,[2] and obtaining sufficient sample sizes to compare multimodal strategies is therefore



VIDEO 5. A polytetrafluoroethylene graft (6 or 8 mm) can be implanted. Video available at: https://www.jtcvs.org/article/S2666-2507(24)00156-1/fulltext.



VIDEO 6. Standard lymph node dissection, including stations 7 to 9 after opening the posterior mediastinum and pulmonary ligament. Video available at: https://www.jtcvs.org/article/S2666-2507(24)00156-1/fulltext.

challenging. No randomized trials have compared neoadjuvant to adjuvant chemoradiation therapy in patients with operable Pancoast tumors. Anterior tumors may be particularly aggressive. In a comparative study, anterior tumors (n = 21) were independently associated with worse survival by multivariate analysis, compared with posterior tumors (n = 71), and the survival benefit associated with a pathologic complete response was significant for anterior tumors but not posterior tumors.[10] Moreover, invasion of the subclavian artery was an independent risk factor for worse survival.[11] Recurrences are more often systemic than locoregional in patients with anterior versus posterior tumors.[10] Thus, the benefits of systemic anticancer therapy may be greatest in patients with anterior tumors.

A major goal of neoadjuvant therapy is to increase the rate of complete en bloc R0 resection. Concurrent chemoradiation therapy followed by surgery is the standard of care for Pancoast tumors in many centers.[12,13] This practice is based on results from two single-arm Phase 2 trials in 88[14] and 57[15] patients. The 5-year survival rates were 54% and 70%, respectively, and pathologic complete response to neoadjuvant therapy was associated with significantly better survival. However, the lack of standardization in classifying Pancoast tumors and their surgical management complicates the interpretation of these findings. In the Intergroup trial,[14] 22 (20%) of the eligible patients refused surgery or died before surgery. Moreover, of the 88 operated patients, 13 underwent pulmonary resection without chest wall resection because marked tumor regression was demonstrated after neoadjuvant therapy and preoperative imaging showed no chest wall involvement. R0 resection was achieved in 83 (94%) patients. Similarly, in the second trial,[15] of the 75 eligible patients given neoadjuvant therapy, only 57 (76%) had surgery, including 6 without chest wall resection and 51 (90%) with R0 resection. An important issue is whether chemoradiotherapy is superior to chemotherapy alone before surgery. The tissue changes caused by preoperative radiation therapy may compromise the ability to perform optimal resection.[16] In a retrospective study, compared with chemotherapy alone for induction, chemoradiation was associated with a significantly higher postoperative complications rate.[16] Thus, selected patients may derive greater benefits from neoadjuvant chemotherapy alone followed by adjuvant radiotherapy.

Consequently, at our institution, when the preoperative workup argues in favor of operability (no N2 or N3 disease, no metastasis, and no brachial plexus involvement higher than C8), we perform upfront surgery followed by adjuvant treatment. Patients with bulky tumors or N2/N3 disease are given 3 cycles of platin-based chemotherapy without radiation therapy and are then reassessed by PET, CTA, and functional tests. Surgery is performed if the response is good (shrinkage of the tumor and decreased radioisotope uptake by PET and for N2/N3 nodes a complete response on PET. In case of decrease of radioisotope uptake, endobronchial ultrasound or scalene node biopsy are repeated to confirm clearance of N2/N3); if not the patient is referred to definitive chemoradiation therapy. In the cohort reported below, only 33% of patients received neoadjuvant therapy, usually consisting in chemotherapy alone, yet the R0 resection rate was similar to that in the 2 above-mentioned studies of neoadjuvant chemoradiotherapy.[14,15] After surgery, we provide adjuvant chemoradiotherapy as needed. Patients with R1 resection receive full-dose radiation therapy with a boost on the target area marked preoperatively by a metallic clip. Adjuvant therapy is not given to patients with wide tumor-free margins and Pn0 disease or to patients with a difficult recovery after surgery.

SURGICAL PROCEDURES AND OUTCOMES AT OUR INSTITUTION

These are detailed in Appendix E1.

CONCLUSIONS AND FUTURE DIRECTIONS

Anterior Pancoast tumors are rare, extremely aggressive malignancies at high risk for systemic dissemination. Multimodal management seems crucial, although its optimal design remains undetermined. Choosing a surgical approach that allows en-bloc R0 resection of the tumor and invaded adjacent structures, and reconstruction of the latter when necessary, is of the utmost importance. With our multimodal personalized strategy, R0 resection was achieved in 90% of patients and 5-year survival was 54%.

The role for immunotherapy or tyrosine kinase inhibitor therapy in Pancoast tumors is being investigated. In NSCLC at any location, neoadjuvant chemotherapy combined with immunotherapy was more effective than chemotherapy alone.[12] A strategy including neoadjuvant chemo-immuno-radiation therapy, surgery, and adjuvant immunotherapy is being assessed in patients with Stage IIIA-B NSCLC.[13] Adding tyrosine kinase inhibitor therapy in patients with epidermal growth factor receptor mutations is also under investigation. Studies focused specifically on Pancoast tumors are needed. Local recurrences are rare after surgery for Pancoast tumor, due to the high R0 resection rate, but distant metastases are common and often fatal.[5,7,8,10] Consequently, research aimed at increasing the efficacy of neoadjuvant and adjuvant regimens, notably via the incorporation of immunotherapeutic agents, is urgently awaited.

Conflict of Interest Statement

The authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling manuscripts for which they may have a conflict of interest. The

editors and reviewers of this article have no conflicts of interest.

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Key Words: Pancoast tumors, anterior, surgery

APPENDIX E1. SURGICAL PROCEDURES AND OUTCOMES FOR ANTERIOR PANCOAST TUMORS AT OUR INSTITUTION

Study Design

We conducted a retrospective observational study of consecutive patients with non–small cell lung cancer involving the thoracic inlet who underwent curative-intent surgery at the Marie Lannelongue Hospital (Le Plessis-Robinson, France) between January 2000 and December 2022. The institutional review board approved the study (Cerc-ctcv-2024-01-26_33230) and waived the need for informed consent in compliance with French law on retrospective studies of anonymized health data.

Data Collection

The study data were collected into an electronic database by members of the surgical team. The following were recorded for each patient: baseline characteristics, features of the tumor, characteristics of the surgical procedure, margins, neoadjuvant and adjuvant treatments, and survival at 3 months and at last follow-up.

Local recurrence was defined as tumor recurrence located in the surgical field, ipsilateral chest, or mediastinum and diagnosed by radiography or histology. Operative mortality was defined as death within 90 days after surgery or before hospital discharge.

Statistical Analysis

Continuous variables are described as mean ± SD or median and range and categorical variables as n (%). Comparisons were with the unpaired 2-tailed *t* test for continuous variables and χ^2 test or Fisher exact test for categorical variables. Overall survival was defined as the length of time from surgery to death or last follow-up and overall disease-free survival as the time from surgery to recurrence of tumor or death or last follow-up without tumor recurrence. Survival after surgery and disease-free survival were evaluated using the Kaplan-Meier method, with comparisons using the log-rank test. All statistical analyses were run on Statview V (Abacus Concept).

Results

Patients and procedures. During the study period, 192 patients underwent surgery for Pancoast tumors. Among them, 54 had a posterior tumor and 65 had spinal involvement. Seventy-three patients with anterior Pancoast were included in the study. There were 52 men and 21 women, with a mean age of 57 years (range, 31-80 years) (Table E1).

Neoadjuvant treatment was given to 24 (33%) patients and consisted in platinum-based chemotherapy alone (n = 18) or with radiation in a mean dose of 40 Gy (range, 30-50 Gy) (n = 6). This treatment was given either before referral to our institution (n = 14, including all 6 patients who received neoadjuvant radiation therapy) or for an extensive tumor (n = 10, all of whom received three cisplatin-based cycles). After induction therapy, positron-emission tomography-computed tomography, computed tomography, and magnetic resonance imaging of the head, neck, and chest were performed routinely to rule out disease progression.

The tumor was on the right side in 44 (60%) patients. After rib resection, no chest wall reconstruction was performed. The T1 root was involved and resected in 24 patients, the C8 root in 2 patients, and the phrenic nerve in 55 (75%) patients. Two patients had superior vena cava involvement, which was managed by resection and reconstruction using a polytetrafluoroethylene graft. In 45 (62%) patients, the subclavian artery was involved. In 1 of them, the tumor extended to the innominate artery. Revascularization was performed by end-to-end anastomosis (n = 34) or polytetrafluoroethylene graft implantation (n = 11) through the transcervical approach.

The subclavian vein and vertebral artery were resected in 52 (71%) patients and 8 (11%) patients, respectively, and were not reconstructed. Lung resection consisted of a standard lobectomy in 70 (96%) patients and sleeve lobectomy in 3 (4%) patients and was followed by mediastinal lymphadenectomy. The most common histological types were adenocarcinoma (n = 43 [59%]) and squamous-cell carcinoma (n = 29 [40%]). One patient had a large-cell carcinoma. Median tumor size was 5.7 cm (range, 1.5-11 cm). Frozen sections of the distal margins of the tumor-bearing areas were examined intraoperatively.

The final histologic evaluation showed complete microscopic resection (R0) in 66 (90%) patients and microscopic tumor invasion (R1) in 7 patients with residual tumor in the brachial plexus (n = 6) or trachea (n = 1). The final node classification was N3 (supraclavicular) in 7 (10%) patients, N2 in 3 (4%) patients, N1 in 9 (12%) patients, and N0 in 54 (74%) patients.

Operative mortality was 2.7%: 2 patients died from pneumonia. Major postoperative complications occurred in 21 (29%) patients, the most common being pneumonia due to phrenic nerve palsy (Table E2).

Adjuvant treatments and long-term outcomes. Adjuvant platinum-based chemotherapy was given alone or with radiation therapy to 13 and 31 patients, respectively. Three patients received adjuvant radiotherapy alone. The median cumulative radiation dose was 45 Gy (range, 30-60 Gy).

No patient was lost to follow-up. Recurrences were seen in 33 (45%) patients and were local in 6 (8%) patients, systemic in 25 (34%) patients, and both in 2 (3%) patients. Median overall survival was 65 months. Overall 3-, 5-, and 10-year survival rates were 58%, 54%, and 49%,

respectively (Figure E1). The 3-, 5-, and 10-year disease-free survival rates were 50%, 48%, and 41%, respectively. Six (8%) patients were alive and free of disease 10 years after surgery. By univariate analysis, factors associated with poorer survival were R1 resection ($P = .036$) and N2 or N3 nodal status ($P = .01$) (Table E1).

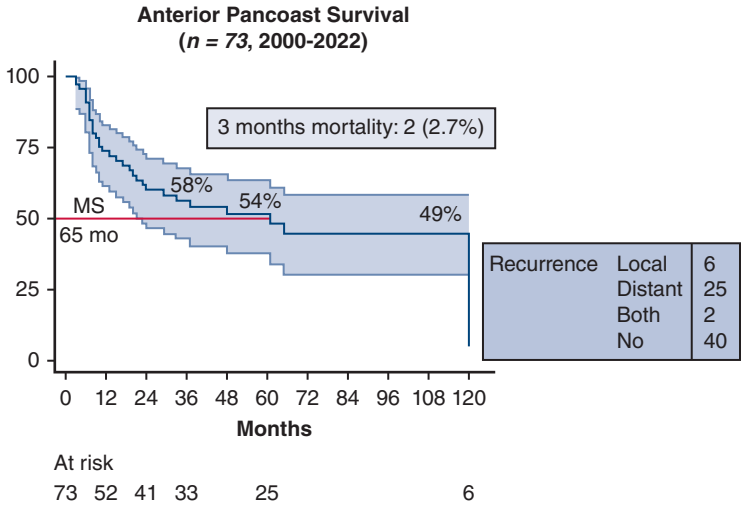

FIGURE E1. Kaplan-Meyer survival plot after surgery for Pancoast tumor. *MS*, Median survival.

TABLE E1. Assessment of factors potentially associated with survival in patients with anterior Pancoast tumors

Factor	Result	*P* value
Male/Female	52 (71)/21 (29)	.68
Age (y)	58 (31-80)	.85
T status, n		
T2/T3	35 (48)	.31
T4	38 (52)	
Nodal status, n		
N0/N1	63 (86), 54/9	.01
N2/N3	10 (14), 3/7	
Neoadjuvant therapy		.82
Yes	24 (33) (Ch 18, CRT 6)	
No	49 (67)	
Resection margins		.036
R0	66 (90)	
R1	7 (10)	
Adjuvant therapy		.86
Yes	47 (64) (Ch 13, RT 3, both 31)	
No	26 (36)	
Subclavian artery involved		.47
Yes	45 (62)	
No	28 (38)	

Values are presented as n (%) or mean (range). *Ch*, Chemotherapy; *CRT*, chemoradiotherapy; *RT*, radiotherapy.

TABLE E2. Postoperative complications in patients with anterior Pancoast tumors

Complication	N	Deaths
Pneumonia	19	2
Acute pulmonary embolism requiring surgical thrombectomy	1	–
Wound breakdown	1	–
Pyothorax requiring revision surgery	1	–
Bleeding requiring revision surgery	4	–
Chylothorax requiring revision surgery	1	–
Total		2 (2.7)

Values are presented as n or n (%).