Surgical Treatment of Superior Sulcus Tumors*
Results and Prognostic Factors

Marco Alfano, MD; Massimiliano D’Aiuto, MD; Pierre Magdeleinat, MD; Eric Poupardin, MD; Aziz Chafik, MD; Salvatore Strano, MD; and Jean François Regnard, MD

**Objectives:** To study the clinical characteristics, treatment modalities, and outcome of patients with superior sulcus tumors who underwent surgery over a 15-year period.

**Design:** Retrospective clinical study.

**Methods:** Clinical records of all patients operated on for superior sulcus tumors by the same surgical team between 1988 and 2002 were reviewed retrospectively.

**Results:** Sixty-seven patients were operated on in this period. All the patients underwent en bloc lung and chest wall resection. Surgical approaches were as follows: posterolateral thoracotomy according to Paulson (n=33), combined transcervical and transthoracic approach (n=33), and isolated transcervical approach (n=1). Types of pulmonary resection included lobectomies (n=59), pneumonectomies (n=2), and wedge resections (n=6). Pathologic stages were IIB, IIIA, and IIIB in 49 cases, 12 cases, and 6 cases, respectively. Resection was complete in 55 patients (82%). Operative mortality was 8.9% (n=6). Postoperative treatment was administered in 53 patients (radiotherapy, n=42; chemoradiotherapy, n=9; and chemotherapy, n=2).

Overall 2-year and 5-year survival rates were 54.2% and 36.2%, respectively. Five-year survival was significantly higher after complete resection than after incomplete resection (44.9% vs 0%, p = 0.000065). The presence of associated major illness negatively affected the outcome (5-year survival, 16.9% vs 52%; p = 0.043). Age, weight loss, respiratory impairment, tumor size, presence of nodal disease, and histologic type did not influence the long-term outcome. At multivariate analysis, only the completeness of resection and the absence of associated major comorbidities had an independent positive prognostic value.

**Conclusions:** Superior sulcus tumor remains an extremely severe condition, but long-term survivals may be achieved in a large percentage of cases. The presence of associated major illness and the completeness of resection are the two most important factors affecting the long-term outcome.

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**Key words:** chest wall; lung cancer; Pancoast tumor; prognostic factors; superior sulcus; surgery

**Abbreviation:** $V_O^2$ = oxygen uptake

Superior sulcus tumors are rarely encountered in clinical practice, representing < 5% of all bronchogenic carcinomas. In 1932, Pancoast published his classic article in which he reported four patients who had a similar presentation including pain in the shoulder and arm, weakness and wasting of the muscles of the hand, and ipsilateral Horner syndrome together with a lesion situated at the apex of the lung. Pancoast rejected the pulmonary origin of the tumor that was recognized by Tobias, who described the same clinical syndrome in four other patients.

Superior sulcus tumors are not necessarily associated with the classic Pancoast syndrome. Though some controversy exists about their exact definition, it is generally accepted that they may be defined as primary lung cancers involving the apex of the chest wall and usually associated with pain in the shoulder and/or arm. Invasion of one or more of the following structures is frequent: lower roots of the brachial plexus, stellate ganglion and...
sympathetic trunk, upper thoracic ribs or vertebralae, subclavian vessels.\textsuperscript{4,5}

The prognosis of this tumor remained poor until 1961 when Shaw et al\textsuperscript{6} reported their satisfactory experience with a bimodality treatment based on preoperative radiotherapy followed by surgery through a posterior thoracotomy approach. Several other reports\textsuperscript{1,5-11} confirmed that 5-year survivals of approximately 10 to 35\% could be achieved with this combined approach, which became the standard treatment. Although radiotherapy was performed prior to surgery in most series, in the experience of others\textsuperscript{12,13} it was often carried out postoperatively. To date, no definitive data about preferable timing exist.

The approach of Paulson\textsuperscript{7} is completely satisfactory in dealing with posteriorly located tumors; however, it is not fully adequate in the presence of invasion of anteriorly located structures (especially subclavian vessels or their branches). Therefore, different anterior approaches have been developed in the last 25 years, including the cervicosternothoracotomy\textsuperscript{14} or the hemi-clamshell incision,\textsuperscript{15,16} the transcervical-transthoracic approach with resection of the clavicle,\textsuperscript{12,17} and the transmanubrial approach.\textsuperscript{18} Exact indications for these different approaches remain controversial, and few data are available about long-term outcome of patients treated by anterior approaches.\textsuperscript{12,13,16}

In the present study, we retrospectively reviewed the clinical features and the management of 67 patients with superior sulcus non-small cell lung cancer referred to us for surgery in a 15-year period. Preoperative workup, choice of operative technique, results, and prognostic factors are presented and discussed.

**Materials and Methods**

We retrospectively reviewed the clinical records of all 67 patients who underwent surgery with a curative intent for superior sulcus non-small cell lung cancer in a 15-year period (September 1988 to April 2002). Preoperative evaluation for all patients included their history, physical examination, routine blood tests, ECG, spirometry, and perfusion lung scan. Staging protocol for all cases included chest radiography, fiberoptic bronchoscopy, and thoracic, upper-abdominal, and cerebral CT scan. Isotopic bone scanning was performed in the presence of extrathoracic bone pain and/or abnormalities in serum calcium or alkaline phosphatase. Standard angiography or MRI were not routinely employed.

Resection was considered functionally possible without further investigations if the predictive postoperative FEV\textsubscript{1} (calculated on the basis of spirometry and isotopic scan) was \geq 40\% of predicted FEV\textsubscript{1} and provided that no major hypoxemia (< 60 mm Hg) or hypercapnia (> 46 mm Hg) existed. Otherwise, an exercise test with determination of maximum oxygen uptake (V\textsubscript{O\textsubscript{2}}) was performed. Operative risk was considered acceptable if the maximum V\textsubscript{O\textsubscript{2}} was \geq 20 mL/kg/min and unacceptable if it was \leq 10 mL/kg/min. In the presence of values between 10 mL/kg/min and 20 mL/kg/min, patients were considered at relatively high risk and definitive decision was based on a complex evaluation taking into account the predictive postoperative FEV\textsubscript{1}, P\textsubscript{O\textsubscript{2}}, P\textsubscript{CO\textsubscript{2}}, maximum V\textsubscript{O\textsubscript{2}}, age, and associated comorbidities; therefore, no strict criterion was followed. In these cases, the possibility of performing a sublobar resection was considered.

Before 1990, patients with suspicion of limited N2 disease were judged immediately operable provided that no bulky disease existed. After this date, in the presence of enlarged (> 1.5 cm) mediastinal nodes, mediastinoscopy was performed. If N2 disease was confirmed, neoadjuvant chemotherapy was administered. Subsequent surgery was undertaken if there was an objective response or no disease progression.

Since the beginning of our series, the opportunity of performing an anterior approach was evaluated. Indications for anterior approaches were as follows: (1) presence of a palpable supraclavicular mass, (2) clinical involvement of C7 and/or C8 root, (3) Horner syndrome, and (4) proven or suspected vascular infiltration. The transclavicular approach\textsuperscript{12,17} was employed up to 1997, and the transmanubrial approach\textsuperscript{18} was used thereafter. Lobectomy constituted the standard pulmonary resection. Sublobar resections were carried out only in the presence of severe respiratory impairment. Chest wall resection was performed en bloc with the lung parenchyma. Nodal dissection was routinely carried out.

The same surgical team operated on all the patients, at the Marie Lannelongue Surgical Center (Le Plessis Robinson, France) up to October 2000 and at the Hotel-Dieu Hôpital (Paris, France) thereafter. Radiotherapy or chemotherapy were performed under the care of referring physicians, so no uniform protocol was employed.

Operative mortality was calculated by taking into account all the deaths occurring within 30 days from the operation or during the hospitalization. Survival rates, including noncancer-related deaths, were calculated by the Kaplan-Meier method and compared by the log-rank test.

Age, weight loss, associated major comorbidities (as defined as chronic cardiac insufficiency, ischemic heart disease, and other vascular occlusive disease, all requiring long-term treatment), respiratory impairment, tumor size, nodal disease, histologic type, and completeness of resection were evaluated by univariate and multivariate analysis. (Cox proportional hazard model). Results were considered significant if the p value was < 0.05.

**Results**

Sixty-seven patients with potentially resectable superior sulcus non-small cell lung cancer were operated on during the study period. There were 57 men and 10 women; mean age was 51 years (range, 21 to 71 years; 15 patients were > 65 years old). Major comorbidities were present in 16 patients (chronic cardiac insufficiency, n = 2; ischemic heart disease, n = 8; and other vascular occlusive disease, n = 6).

**Symptoms**

All the patients had chest and/or shoulder pain. Severe and steady pain along the distribution of the seventh and/or the eighth cervical and/or the first thoracic nerve root was present in 51 patients (T1,
respectively. Mortality rate was 3% in patients operated on by posterior approach, as compared to 15% in patients operated on by combined anterior and posterior approach.

Pathologic Examination

There were 23 squamous cell carcinomas, 34 adenocarcinomas, 6 large cell carcinomas, and 4 mixed cellularity carcinomas. Pathologic stages were T3N0 in 49 patients (73%), T3N1 in 6 patients (9%), and T3N2 in 6 patients (9%). In six patients (9%), a T4 stage was recognized. Causes of T4 disease were (isolated or associated): vertebral body involvement (n = 3), satellite tumoral nodule (n = 2), subclavian vein involvement (n = 2), and subclavian artery involvement (n = 2). Nerve root invasion was confirmed in all the 18 patients who had undergone its resection.

A pathologically completed resection was achieved in 55 cases (82%). Pathologic stages in these cases were T3N0, T3N1, T3N2, and T4N0 in 42, 6, 4, and 3 patients, respectively. Resection was not complete in 12 patients: microscopic residual disease was found in 6 patients at pathology, whereas in the remaining 6 patients the resection was macroscopically not complete.

Postoperative Treatments

Among the 61 patients who survived the operative period, 53 patients underwent postoperative treatments: radiotherapy (n = 42), chemoradiotherapy (n = 9), and chemotherapy (n = 2). In particular, after complete resection, a postoperative treatment was administered in 46 of 50 patients (radiotherapy, n = 38; chemoradiotherapy, n = 7; and chemotherapy, n = 1), whereas after incomplete resection, 7 of 11 patients underwent postoperative treatments (radiotherapy, n = 4; chemoradiotherapy, n = 2; and chemotherapy, n = 1). In four patients with incomplete resection, the planned postoperative treatment could not take place for death due to unrelated cause (n = 1), rapid metastatic disease (n = 2), and patient refusal (n = 1). Mean postoperative radiotherapy dose was 55 Gy (range, 10 to 65 Gy).

Survival

At completion of the study, 25 patients were alive and disease free and 2 patients were alive but with tumor relapse with a mean follow-up of 50 months (range, 3 to 176 months). There were 34 late deaths, 27 tumor related and 7 due to unrelated causes.

Two-year and 5-year survivals for the whole population were 54.2% and 36.2%, respectively (Fig 1). Two-year and 5-year survival rates were significantly higher after complete resection (64% and 44.9%, respectively).
respectively) than after incomplete resection (12.1% and 0%, respectively; \( p = 0.000065 \); Fig 2). Following complete resection, local recurrence occurred in 5 of 50 evaluable patients (10%); in 3 of these patients, it was associated to metastatic spread. All 12 patients who had an incomplete resection acquired local tumor progression or metastatic disease.

Prognostic factors were evaluated in the 50 completely resected patients. Five-year survival was 46% in T3 patients receiving a complete resection (47.7% in T3N0 disease) [Fig 3]. The only patient with T4 disease who received a complete resection and survived the postoperative period died of metastatic disease 9 months postoperatively.

A significantly lower 5-year survival was observed in patients with associated major comorbidities (16.9% vs 52%, \( p = 0.043 \); Fig 4). No difference was found in terms of 5-year survival between patients without nodal disease and those with nodal involvement (47.7% in N0 vs 50.6 in node-positive, not significant). The low number of subjects in each group of nodal disease (N1 and N2) precludes a separate analysis. Five-year survival was not significantly higher in patients aged < 65 years (46.7%) as compared with patients aged > 65 years (38.9%) \( [p = 0.72] \). Weight loss, respiratory impairment, tumor size, histologic type, and extent of chest wall resection (number of ribs) did not affect long-term survival. At multivariate analysis, only the completeness of resection and the absence of associated major comorbidities had an independent positive prognostic value (\( p = 0.00027 \) and \( p = 0.0069 \), respectively).
DISCUSSION

Superior sulcus tumor is a relatively unusual condition. We operated on 67 subjects in a 15-year period. In our experience, there was a strong preponderance of men (57 men vs 10 women). This is in contrast with North American studies, but in complete agreement with European studies and probably reflects the different tobacco habits in the two continents.

Management of patients with superior sulcus tumors is still considered a challenge due to the aggressiveness of the disease, the delicate anatomy of the region, the difficulties (and the controversies) in the choice of the surgical approach. There is general agreement that an extensive preoperative workup is required. As authoritatively outlined, CT scan plays a fundamental role in assessing locoregional extension. In our patients, angiography and MRI were not routinely employed, but were frequently performed in the presence of doubts about vascular involvement at contrast-enhanced CT scan. This approach was helpful in selecting patients requiring an anterior approach, but never disqualified the operative indication.

Several patients in our series had no preoperative histologic diagnosis, in spite having undergone bronchoscopy. Mediastinoscopy was not routinely carried out. A small percentage of patients were found to have N2 disease at surgical nodal dissection; therefore, routine mediastinoscopy would have provided a preoperative histologic diagnosis in only a small number of patients. Percutaneous needle biopsy was performed under the care of referring physicians in only 15 patients; this clearly reflects the strong restriction of the use of this technique by most French surgical teams, with the idea (clearly debatable) that a negative result of percutaneous needle biopsy would not contraindicate surgery.

As always in patients with lung cancer, preoperative staging is of fundamental importance. Since the beginning of 1990, we perform mediastinoscopy in the presence of enlarged mediastinal nodes and administer neoadjuvant chemotherapy if N2 disease is confirmed. This occurred in few patients in our series. In the initial period of the study (from September 1988 to September 1989), patients with limited clinical N2 disease (as established on the basis of CT scan) were considered immediately operable provided that no bulky disease existed. Unfortunately, the number of patients with limited clinical N2 disease in the initial part of the study is too low to perform a comparison with patients in the second part of the study, so it is impossible to speculate if the change in the strategy resulted in increased resectability (and, possibly, survival).

Despite the progress in anesthesia techniques, pain control and management of postoperative complications, the operative mortality remains high. We observed a mortality rate of 8.9%. This figure can be considered consistent with those found in literature. For comparison, it was 4% in the experience of Rusch et al, 5% in the series by Maggi et al, 7.2% according to Martinod et al, but 14% according to Wright and coworkers. This variability probably depends on differences in studied populations and operative techniques. Of note, in our experience mortality was remarkably higher when a double approach was used (15%) than after operations performed only through the posterior approach (3%). It is noteworthy that almost all the series published so far dealt with patients operated on through the classical posterior approach.

Long-term results were satisfactory in this advanced-stage lung cancer. In our study, overall 2-year and 5-year survivals for the whole population were 54.2% and 36.2%, respectively. These figures were significantly higher after complete resection (64% and 44.9%, respectively) than after incomplete resection (12.1% and 0%, respectively). There is wide variability in overall 5-year survival rates reported in larger series, with figures ranging 10 to 35% probably because of the heterogeneity in studied populations, operative techniques, and preoperative and postoperative treatments. Such heterogeneity is probably responsible for the difference in the percentage of T3 and T4 tumors as well as in the rates of complete resection. Comparison of long-term results of different studies is difficult also for the frequent lack of information about survival according to the pathologic stage. In our series, 5-year survival was 46% in patients with T3 tumors receiving a complete resection and 47.7% in T3N0 disease. Few data are available about the outcome of this subset of patients with superior sulcus tumor; our values are similar to those reported by Rusch et al, who showed a 5-year survival of 46% in patients with stage IIB tumors.

We observed that completeness of resection was a factor influencing survival as demonstrated by univariate and multivariate analysis, a finding common to other series. In our experience, there were no long-term survivors among patients who had received an incomplete resection; however, if a complete resection could be achieved, a definitive local control of the disease was observed in 90% of cases.

Complete resection was possible in 82% of patients. This percentage compares favorably with the majority of series in which this result is shown: 53%, 56%, and 60%, respectively, in the experience of Rusch et al, Ginsberg et al, and Maggi et al.
these three series deal with > 60 patients. However, Devine et al.\(^9\) and Martinez-Monge et al.\(^{25}\) reported rates of 70% and 76%, respectively, in two series dealing with a smaller number of subjects. We think that patient selection is probably the main cause of these discrepancies, but the type of surgical approach is probably another important factor. As already stated, in the great majority of published studies,\(^ {5,11,19,23-25}\) the classical posterior approach described by Shaw et al.\(^6\) was utilized. Since the beginning of the study, we use anterior approaches (the transclavicular one was employed up to 1997 and the transmanubrial approach thereafter) in the presence of a palpable supraclavicular mass, and/or clinical involvement of C7 and/or C8 root, and/or Horner syndrome, and/or proven or suspected vascular infiltration. A classical posterolateral thoracotomy was added in all but one case. It is noteworthy that there is no established criteria for determining the optimal surgical approach, and few data are available about this subject. The exclusive posterior approach continues to be employed by most authors; however, Grunenwald and Spaggiari\(^{18}\) and Vanakesa and Goldstraw\(^{26}\) suggest a systematic combined approach, while Dartevelle et al.\(^{12}\) do not provide strict recommendations. The choice of surgical approach should be adapted to individual cases and should take into account the above-mentioned criteria. We observed that the combined anterior and posterior approach was associated with a high mortality, and this combined approach should be used only if preoperative workup shows that the classical posterior approach will be inadequate in dealing radically with the disease.

The small percentage of T4 tumors in our series (9% of all tumors) is probably the other factor explaining the high rate of complete resection; this small percentage probably reflects the selection criteria of our surgical candidates. In agreement with other authors,\(^ {12,23,24}\) in our experience patients with massive vertebral involvement were considered inoperable and only three patients with limited vertebral involvement underwent surgery; however, in some surgical series, involvement of vertebral body (also massive) was not considered a contraindication for surgery.\(^ {5,13,19,20}\) However the possibilities of achieving a complete resection in these cases are probably poor. Few data are available about completeness of resection in patients with superior sulcus tumor and vertebral body involvement. In the study of Rusch et al.\(^{19}\) including 55 patients with T4 superior sulcus tumors, vertebral body involvement was the cause of the T4 staging in 34 cases (62%). Though the rate of complete resection in this subset of patients is not stated, it was probably low, as among all patients with T4 lesions, a complete resection could be achieved in only 20 cases (36%).

Only four patients in our series had tumor infiltration of subclavian vessels deeper than the adventitial layer; they represented 5.9% of the whole population. This percentage is similar to that recently reported by Martinod et al.,\(^{13}\) but lower as compared to the experience of others.\(^ {5,12}\) Although we observed that tumor invasion of subclavian vessels deeper than the adventitial layer was uncommon, infiltration limited to the vascular adventitia was a frequent feature. As already suggested,\(^{13}\) in these cases subadventitial dissection allowed a complete excision while avoiding the resection of a great vessel; however, tumor infiltration of collateral branches of subclavian artery was common in our series, occurring in 16 cases. In these cases, their resection was obviously necessary. The anterior approaches were extremely useful in dealing safely and satisfactorily with this subset of superior sulcus tumors.

Dissection of tumor from nerve roots was often possible, and a fully satisfactory neurolysis could be achieved in most cases; however, in 18 patients, nerve root resection was necessary. This obviously resulted in a neurologic deficit in the territory of distribution (generally already present preoperatively), but never caused a strong functional disability.

We are not able to provide long-term results of surgery for T4 superior sulcus tumors. In our series, the only patient with T4 disease who received a complete resection and survived the postoperative period died of metastatic disease 9 months postoperatively. Though the number of patients with T4 tumors included in our series is extremely low to draw any conclusion, we think that selection of surgical candidates among patients with tumors classified T4 at preoperative workup should be particularly rigorous. There are few data in literature about the long-term outcome of patients with T4 superior sulcus tumors treated by surgery, but some authors have reported a small percentage of long-term survivors in this subset of patients. Rusch et al.\(^{19}\) reported 5-year survival rates of 13% in patients with superior sulcus stage III B tumors (a group including some patients with T3N3 disease), whereas in the experience of Wright et al.\(^{5}\) there were some 2-year survivors among the nine patients with T4 tumors; however no longer follow-up was available. In addition, according to others,\(^ {20}\) the outcome of T4 superior sulcus tumors was constantly unfavorable.

In our experience, nodal disease was found in 12 patients (N1, n = 6; N2, n = 6). The low percentage of patients with nodal disease in our series is similar to that found by other authors,\(^ {13,23}\) who used similar presurgical staging protocols, thus confirming that in spite of an aggressive local behavior, regional spread-
ing to nodes is not a frequent feature of superior sulcus tumors. Of note in our experience, disease could not be understaged at surgery as full nodal dissection was routinely carried out. Ten of 12 patients with nodal disease could undergo complete resection. Five-year survival was 50.0%, a figure similar to that found in the absence of nodal disease. Unfortunately, the small number of subject in each group precludes a separate analysis. Among the four patients with N2 disease who underwent a complete resection, two patients are currently alive (at 1-year and 7-year follow-up, respectively) and two patients died 8 months and 14 months after the operation, respectively. Few data are available in literature about the outcome of patients with N2 superior sulcus tumor: Maggi et al. found no differences in survival between patients with and without mediastinal nodal disease, whereas in the experience of Rusch et al., mediastinal nodal involvement negatively affected the outcome. The number of our patients with N2 disease is extremely limited, so no recommendation can be drawn from our results; however, we think that preoperative recognition of N2 disease should not necessarily be considered a definitive contraindication to surgery, the inclusion of such patients in protocols of induction treatments is probably justified. We would like to outline that we have previously reported a 5-year survival of 21% in lung cancer involving chest wall in the presence of N2 disease, another condition also often considered as a definitive contraindication to surgery.

At both univariate and multivariate analysis a significantly lower 5-year survival was observed in patients with associated major illness (16.9% vs 52%, p = 0.043). Although this factor has not been specifically evaluated in surgical series dealing with superior sulcus tumor, it has been shown to negatively affect the long-term outcome in surgical series of patients with early stage lung cancer.

Differently from the great majority of other series, in our experience few patients underwent preoperative radiotherapy, whereas almost all underwent postoperative radiotherapy. Dose administration was largely variable, as our institution is a tertiary referral center and the patients included in this study were under the care of a great number of physicians with different opinions in terms of adjuvant treatments. Although in other reports a similar treatment strategy was often adopted, it is generally believed that preoperative radiotherapy would facilitate surgical resection, increase the percentage of complete resections, and achieve better long-term results. As already stated, in our experience the rate of complete resection was fully satisfactory and difficulties in dissection were generally similar to those usually encountered when operating on locally advanced lung cancers. Furthermore, although comparison of long-term outcomes is difficult, our results seem to compare favorably with the experience of others. We have generally employed a treatment strategy based on immediate surgery and adjuvant treatments (provided that the tumor was judged completely resectable at preoperative workup) with the idea that this strategy would offer the possibility of immediate disease (and symptoms) control while avoiding the risks of delaying or annulling surgery for radiotherapy-induced complications; however, in four patients treated with induction chemoradiation, tumor resectability at presentation was debated. Neoadjuvant treatment achieved down-staging in all these cases, and a complete resection was possible.

A treatment strategy based on induction chemoradiation is currently under investigation. Extremely encouraging results have been reported in a small retrospective series by Wright et al. Rusch and associates have reported the initial results of a phase II multicenter trial including patients with no mediastinal nodal involvement; in this trial, the mortality due to induction chemoradiation was relatively low (2.7%), but only 75% of initially enrolled patients could undergo surgery. The rate of complete resection was as high at 92%, and 2-year survival was 55% for all eligible patients and 70% for patients who underwent a complete resection. Long-term results are not yet available.

Superior sulcus tumors remain an extremely severe condition, but cure may be achieved in a large percentage of cases. The surgical approach should be adapted to the different clinical and radiologic presentations in order to achieve a complete surgical resection, which represents the most important positive prognostic factor. Surgery carries a high operative risk, especially if a combined approach is needed, so every effort should be made to identify patients expected to derive a benefit that outweighs risks. Prospective randomized trials are needed to indicate the optimal association and timing of surgery, radiotherapy, and chemotherapy. The impact of neoadjuvant treatments on long-term outcomes will constitute a particularly intriguing subject.

REFERENCES


Clinical Investigations

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