Survival after Trimodality Treatment for Superior Sulcus and Central T4 Non-small Cell Lung Cancer

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**Introduction:** For sulcus superior tumors and central cT4 tumors, low resectability and poor long-term survival rates are obtained with single-modality treatment.

**Methods:** Analysis of all consecutive patients in our prospective database, who had potentially resectable superior sulcus (cT3–T4) and central cT4 tumors and were treated with induction chemoradiation (two courses of cisplatin-etoposide) and concomitant radiotherapy (45 Gy/1.8 Gy) after multidisciplinary discussion. Surgery with attempted complete resection was performed in patients showing response or stable disease on computed tomography.

**Results:** Between April 2002 and February 2008, 32 consecutive patients were enrolled. Two patients did not complete the induction chemoradiotherapy. Thirty patients were reassessed after induction, 28 had response or stable disease by conventional imaging. Twenty-seven patients were surgically explored since one patient became medically inoperable during induction treatment. The overall complete resectability was 78% (25/32). Resection was microscopically incomplete (R1) in two patients. In 11 patients (41%), a pneumonectomy was performed, and in 14 patients (52%), a chest wall resection was necessary. In 74% of the resected patients, there was a complete pathologic response or minimal residual microscopic disease. The mean postoperative hospital stay was 9.2 days with no hospital mortality and no bronchopleural fistula. With a median follow-up of 26.5 months, 5-year survival rates are 74% in the intent-to-treat population (n = 32) and 77% in completely resected patients (n = 25), with no statistically significant difference between sulcus superior tumors and centrally located T4 tumors.

**Conclusion:** In patients with sulcus superior tumors and in selected patients with centrally located T4 tumors, trimodality treatment is feasible with acceptable morbidity and mortality. The complete resectability is high, and long-term survival is promising.

**Key Words:** Lung cancer, Superior sulcus, T4, Trimodality treatment, induction therapy.

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**T**umors of the superior sulcus and central T4 tumors are an uncommon subset of non-small cell lung cancer (NSCLC). If surgery is performed, a major problem is to obtain a complete resection with clear margins. In superior sulcus tumors, there is the proximity of critical structures, such as the spine, brachial plexus, and subclavian artery. These structures are difficult to approach technically and they limit the extent of resection. Shaw et al.1 and Paulson2 showed that preoperative radiotherapy resulted in a higher complete resectability rate. Nevertheless, complete resection was achieved in only 60% of the patients, and the overall 5-year survival remained 30%.3 Primary surgery for centrally located T4 tumors disease is unrewarding. A Japanese study showed that complete resection was possible in only one third of the patients, with a hospital mortality as high as the predicted 5-year survival (13%).4

Based on the improved results of induction chemoradiotherapy followed by surgery for superior sulcus tumors5 and stage III disease,6,7 we started trimodality treatment for sulcus superior and central T4 tumors in 2002. The aim of this study was to analyze our results with trimodality treatment in these patients.

**PATIENTS AND METHODS**

We analyzed the results in our prospective database of all consecutive patients treated in our hospital with pathologic proven superior sulcus tumor and centrally located clinical T4 tumors between April 2002 and February 2008. Sulcus superior tumors were defined as tumors located at the top of the lung with involvement of the apical chest wall above the level of the second rib.8 Patients with central tumors had a clinical T4 status (cT4N0–N1) based on their central location, not on satellite nodules, malignant pleural effusion, or carinal involvement. Particular attention was given in patients with superior sulcus tumors to verify the pretreatment T-status, making certain that tumors were coded as T4 only if imaging studies clearly documented spine or subclavian vessel invasion or in case of Horner...
syndrome. In centrally located T4 tumors, clinical staging of the T-factor was based on computed tomography (CT) or magnetic resonance imaging (MRI).

Eligibility criteria included a World Health Organization performance status of 0–1, age <75 years, and a predicted forced expiratory volume in 1 second higher than 40%. Patients had to be able to tolerate cisplatin-based chemotherapy. Patients were excluded if they were not potential surgical candidates on medical grounds. All patients were fully informed about the nature and the purpose of the present study by a pulmonologist/thoracic surgeon and gave informed consent before the start of the treatment. This procedure in general, as well as the analysis of the cohort of this article, was approved by the institutional review board.

All patients were carefully screened for distant metastasis. In short, this consisted of a thorough clinical examination and history, blood tests, including a complete blood count, serum calcium, and liver function tests. All patients had a contrast-enhanced CT-scan of the thorax and upper abdomen. Bone scintigraphy was carried out in patients with bone pain, raised alkaline phosphatase, or serum calcium, completed by bone radiographs, bone CT, or bone MRI in case of equivocal findings. Positron emission tomography (PET) or PET-CT scan was routinely performed in these patients. Cervical mediastinoscopy was recommended to exclude mediastinal nodal metastases. The treatment strategy was decided at the weekly institutional lung cancer multidisciplinary meeting.

The chemotherapy and radiotherapy were administered concurrently. Chemotherapy consisted of cisplatin 60 mg/m² on day 1 and day 21, etoposide 120 mg/m² on days 1–3 and days 21–23, both administered intravenously in a 3-week schedule. The total dose of radiation was 45 Gy in fractions of 1.8 Gy in 25 days (5 weeks), starting on day 1 of the first chemotherapy cycle. The radiation target (gross tumor volume, GTV) was defined by CT scan, correlated with PET scan, either visually either on integrated PET-CT. It included the primary tumor and in case of uncertainty regarding the hilar status on CT and/or PET scan, the hilar region was also encompassed within the GTV. The GTV was then enlarged to the planning target volume using an isotropic margin of 1.5 cm. All treatments were planned and delivered with 3D-conformal radiotherapy, according to international accepted guidelines. As the primary aim of this analysis was to look at the results and major complications when using a trimodality approach for NSCLC with borderline T-factor resectability, we did not make a detailed coding of cisplatin-etoposide and radiotherapy, as ample information on this is available. We only registered major safety issues.

Two to 4 weeks after completion of the induction chemoradiotherapy, each case was re-evaluated to determine clinical response according to RECIST criteria and resectability. Re-evaluation included full pulmonary function tests (including diffusion capacity) and CT-scan of chest and upper abdomen. In absence of disease progression (i.e., stable disease or partial complete response [CR]) patients were referred for surgery. Patients found to have progressive disease had other treatment and continued follow-up.

Thoracotomy was undertaken 2 to 4 weeks after completion of the chemoradiotherapy. All surgical procedures were performed by the same team, consisting of anatomic pulmonary resection and systematic nodal dissection.11 The approach was a posterolateral thoracotomy in case of central or superior sulcus tumors, a transmanubrial approach12 in case of an anterior located superior sulcus tumor. Multiple frozen section examinations were used to determine the extent of resection and to evaluate its completeness. For central tumors, the bronchial stump was routinely covered with an intercostal muscle flap. In case of resection of superior sulcus tumors, a pleural flap was used to cover the bronchial stump.

In case of resection, two adjuvant courses of cisplatin and etoposide were administered. In case of incomplete resection, radiotherapy boost was considered.

Final pathology response was divided into three categories: pathologic CR (no residual microscopic tumor), minimal microscopic residual (few scattered foci within mostly necrotic or fibrotic mass), or gross residual tumor (mostly or entirely viable tumor).5

Survival was reported on an intent to treat basis and was defined as time from diagnosis till death or last contact for surviving patients. Survival was calculated according to the Kaplan-Meier method, with difference between groups expressed by the log-rank test.

RESULTS

There were 32 patients with superior sulcus tumors or centrally located T4 tumors planned for this trimodality approach between April 2002 and February 2008. There were 15 patients with superior sulcus tumors, 17 patients had centrally located T4 disease. Table 1 shows the characteristics of these 32 patients. Most patients were men, and squamous cell carcinoma (59%) was the predominant histologic subtype. Two third of superior sulcus tumors were staged as clinical T4 tumors. For centrally located T4 tumors, the list of infiltrated organ is reported in Table 1. Most patients were clinically T4 due to invasion of pulmonary artery (n = 5) or left atrium (n = 5).

The treatment scheme of these patients is shown in Figure 1. In all patients with centrally located T4 tumors and in most patients with superior sulcus tumors (73.3%), cervical mediastinoscopy was performed. In four patients with superior sulcus tumors, no mediastinoscopy was performed because both PET and CT-scan were negative on mediastinal nodes.

Two patients were planned to start trimodality treatment, but did not initiate induction chemoradiotherapy. One patient with superior sulcus tumor developed contralateral pneumonia after invasive surgical staging and was no longer suitable for multimodality therapy. Another patient with centrally located T4 tumor had rapid disease progression with occurrence of malignant pleural effusion and central necrosis of the tumor. This patient received palliative chemotherapy and needed a palliative pneumonectomy for controlling necrosis and infection a few weeks later. This resection was incomplete with positive section margins on the left atrium.
The induction therapy was completed as planned in 30 patients (93.7%). Significant acute toxicity was infrequent. In total, one patient experienced pneumonia, five patients experienced neutropenia (febrile neutropenia: two), and two patients experienced radiation oesophagitis. Three patients needed hospital admission, one for intravenous antibiotics (pneumonia) and two for parenteral nutrition.

Re-evaluation showed disease progression in two patients. Thirteen patients had partial response, and 15 patients had stable disease on imaging and were scheduled for surgery. Functional re-evaluation after induction chemoradiotherapy showed that one patient was not fit enough to undergo surgical resection. This patient was treated by additional radiotherapy.

Twenty-seven patients (84.4%) underwent surgical exploration. The mean time interval between completion of chemoradiotherapy and the surgical intervention was 26 days (range: 16–42 days). Data on the resections performed are summarized in Table 2. In 25 patients, a complete resection was achieved. The intent to treat complete resectability rate was 78.1% for those who underwent surgical exploration it was 92.6%. In two patients, the resection was microscopically incomplete. Both patients had pretreatment a T4 superior sulcus tumors and had microscopic positive margins on the vertebral body.

A pneumonectomy was necessary in 11 patients (right-sided in six). Most of the pneumonectomies were extended resection (intrapericardial or combined with chest wall resection). In 16 patients the resection was confined to lobectomy/bilobectomy. Sleeve resection was performed in two patients. As can be expected, in many patients pulmonary resection with en bloc chest wall resection was performed \( n = 14 \). When the defect was posteriorly located and when there was no risk of entrapment of the scapula, we did not routinely reconstruct the chest wall. Chest wall reconstruction with Gore-Tex 2-mm dual mesh was performed in four patients. The surgical procedures as shown in Table 2 reflect the extent of the disease before the induction chemoradiotherapy. The liberal use of multiple frozen sections could reduce the need

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**TABLE 1. Characteristics of All Eligible Patients \( n = 32 \)**

<table>
<thead>
<tr>
<th>Age (yrs)</th>
<th>Mean (range) 59.5 (47–74)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>Male: 24, Female: 8</td>
</tr>
<tr>
<td>Side</td>
<td>Right: 15, Left: 17</td>
</tr>
<tr>
<td>Histology</td>
<td>Squamous cell carcinoma: 19, Large cell undifferentiated: 8, Adenocarcinoma: 5, Superior sulcus tumors: 15</td>
</tr>
<tr>
<td></td>
<td>cT3: 5, cT4: 10</td>
</tr>
<tr>
<td></td>
<td>Spine: 3, plexus: 4, subclavian artery: 3, Horner: 1</td>
</tr>
<tr>
<td></td>
<td>Centrally located T4: 17</td>
</tr>
<tr>
<td></td>
<td>Pulmonary artery: 5</td>
</tr>
<tr>
<td></td>
<td>Atrium: 5</td>
</tr>
<tr>
<td></td>
<td>Aorta: 3</td>
</tr>
<tr>
<td></td>
<td>Extensive mediastinal infiltration: 2</td>
</tr>
<tr>
<td></td>
<td>Recurrent laryngeal nerve: 1</td>
</tr>
<tr>
<td></td>
<td>Subclavian artery: 1</td>
</tr>
<tr>
<td>Clinical N staging (after invasive staging)</td>
<td>N0: 30, N1: 2, N2: 0</td>
</tr>
</tbody>
</table>

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**FIGURE 1.** Flow diagram showing treatment scheme in 32 patients with centrally T4 tumors or superior sulcus tumors.
for pneumonectomy and proved to be crucial to avoid unnecessary resection of mediastinal structures that seemed macroscopically involved.

In all cases of resection of centrally located tumors ($n = 14$), the bronchial stump was covered with an intercostal muscle flap. After resection of superior sulcus tumors ($n = 13$), the bronchial stump was covered with a broad pleural flap.

Final pathology response showed pathologic CR in three patients, minimal microscopic residual disease in 17 patients, and gross residual tumor in seven patients. In 74% of resected specimens, no or only minimal microscopic vital tumor was found. Table 3 shows the correlation between pathologic and radiologic findings in the 27 patients who underwent resection. Although 15 patients had stable disease on CT, two thirds of them proved to have a major pathologic response with no or only small foci of viable tumor in the resection specimen.

There were no treatment-related deaths. The mean hospital stay was 9.1 days (range: 15–16 days). Fourteen patients (52%) had no postoperative complication. The most observed complications were atrial arrhythmia (15%) and pneumonia (11%) (Table 4). One of the patients with pneumonia had to be admitted to the intensive care for ventilation. In these series, we observed no bronchopleural fistulae or empyema. One patient had a prolonged air leak, one patient developed paralytic ileus, and three patients with superior sulcus tumors experienced clearly more than usual post-thoracotomy pain.

### Consolidation Chemotherapy

In 23 operated patients, two additional courses of consolidation chemotherapy were given 4 to 6 weeks postoperatively. Reasons for not delivering consolidation chemotherapy were poor general condition (1), renal insufficiency (1), unexplained fever (1), and incomplete resection that was treated with additional radiotherapy (1).

Follow-up is complete for all patients. Median follow-up is 26.5 months, median follow-up in patients who are still alive is 33.5 months. At the time of this report, 6 of the 32 patients have died. The overall median survival is not yet reached with an intent to treat ($n = 32$) projected 1-year survival of 93% and a projected 5-year survival of 74% or 77% after complete resection ($n = 25$). We observed a trend of better survival in superior sulcus tumors compared with central T4 tumors (Figure 2). The projected 5-year survival in superior sulcus tumors was 86% and 60% in central T4 tumors ($p = 0.087$).

After resection ($n = 27$), four patients have developed recurrent disease. In two patients with superior sulcus tumors, there was a local recurrence; in the two other patients (7.4%), the brain was the first site of relapse.

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**TABLE 2. Surgical Procedures in 27 Patients**

<table>
<thead>
<tr>
<th>Resectability</th>
<th>Total</th>
<th>R0</th>
<th>92.6%</th>
<th>R1</th>
<th>2</th>
<th>R2</th>
<th>0</th>
</tr>
</thead>
</table>

- Pneumonectomy 11 40.7%
  - Right pneumonectomy 6
  - Standard pneumonectomy 2
  - Intrapericardial pneumonectomy 4
  - Intrapericardial pneumonectomy + chest wall 4
  - Intrapericardial pneumonectomy + left atrium 1
- Lobectomy/bilobectomy 16 60.3%
  - Standard lobectomy 2
  - Sleeve lobectomy 2
  - Lobectomy + subclavian artery 2
  - Lobectomy + chest wall 3
  - Lobectomy + chest wall + processus transversus 3
  - Lobectomy + chest wall + T1 nerve root 4
- Chest wall resection 14
- Chest wall reconstruction 4
- No chest wall reconstruction 10

**TABLE 3. Comparison of Pathological and Radiological Responses in 27 Patients Who were Resected**

<table>
<thead>
<tr>
<th>Radiological Response</th>
<th>Total</th>
<th>Partial Response</th>
<th>Stable Disease</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Pathological response</th>
<th>3</th>
<th>2</th>
<th>1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pathologic complete response</td>
<td>17</td>
<td>8</td>
<td>9</td>
</tr>
<tr>
<td>Minimal microscopic residual disease</td>
<td>Gross residual disease</td>
<td>7</td>
<td>2</td>
</tr>
</tbody>
</table>

**Total** 27 12 15

**TABLE 4. Postoperative Complications in 27 Patients**

<table>
<thead>
<tr>
<th>Type</th>
<th>No Patients</th>
<th>Percent of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atrial arrhythmia</td>
<td>4</td>
<td>15</td>
</tr>
<tr>
<td>Pneumonia (1 admittance to ICU)</td>
<td>3</td>
<td>11</td>
</tr>
<tr>
<td>Intense pain</td>
<td>3</td>
<td>11</td>
</tr>
<tr>
<td>Sputum impaction</td>
<td>2</td>
<td>7.4</td>
</tr>
<tr>
<td>Prolonged air leak &gt;7d</td>
<td>1</td>
<td>3.7</td>
</tr>
<tr>
<td>Ileus</td>
<td>1</td>
<td>3.7</td>
</tr>
</tbody>
</table>

Of the 27 patients who underwent thoracotomy, 14 (52%) had no complications.

ICU, intensive care unit.
DISCUSSION

Primary surgery for superior sulcus tumors or tumors infiltrating by direct extension the mediastinal organs (T4) is unrewarding, as complete resection is not often obtained and 5-year survival is poor. Results of preoperative radiotherapy (30–35 Gy) followed by surgery in 225 patients from Memorial Sloan-Kettering Cancer Centre published by Rusch et al. showed that a complete resection was achieved in only 64% of T3N0 and 39% of T4N0 superior sulcus tumors. An older study from the same center evaluated the results of surgery in NSCLC with direct mediastinal tumor extension who had pN0 or pN1 disease. T3N0 lesion have a more favorable outcome, but still complete resection rate did not exceed 66%. The complete resectability for T4 lesions was only 18% with a 5-year survival of 12%.

Theoretically, an induction program of concurrent chemoradiotherapy seems appropriate for superior sulcus tumors and centrally located T4 tumors. Major problems are often a large, locally infiltrative tumor and the frequent occurrence of distant metastasis. Although superior sulcus tumors and central T4 disease differ in surgical approach and might differ in nodal status, both have in common that a complete resection with clear margins is difficult to obtain because of the proximity of vital structures.

In February 2002, we started our program of trimodality treatment in superior sulcus tumors (T3–T4) and centrally located T4 tumors. Overall, we obtained a complete resectability of 78% and an overall 5-year survival of 74%. We observed similar survival in superior sulcus tumors and centrally T4 tumors although there was a trend of better survival in superior sulcus tumors. Nevertheless, as shown at the bottom of Figure 2, the sample size becomes small when analyzing the subset of superior sulcus tumors and centrally T4 tumors and one should be careful to draw final conclusions.

Our results are very similar compared with the literature, although we realize that our duration of follow-up is rather short to have a solid view beyond 3 years (Table 5). A North American multicenter study enrolled 110 patients with mediastinoscopy negative T3-4N0-1 superior sulcus tumors. The overall complete resectability was 76%. Treatment-related mortality was 4.5%. Pathologic CR or minimally microscopic disease was seen in 61 (56%) of resected specimens. Overall 5-year survival was 44% with a 54% after complete resection.

There are only limited data in the literature of the effect of trimodality treatment in centrally located T4 disease. The largest study was published by Rendina et al. They performed a prospective, single institution study of induction chemotherapy in patients with centrally located, unresectable T4 NSCLC. The complete resectability rate was 63%, and a 5-year survival of 20% was reported. In a subgroup of patients with T4N0, 4-year survival was 58%. Another study evaluated trimodality treatment in 42 patients with stage III disease treated with trimodality treatment. A small subgroup of patients with T4N0 disease (eight patients) had an excellent outcome. Eighty-eight percent of these patients underwent resection. The median survival for

FIGURE 2. Overall survival in cT4 tumors (n = 17) compared with sulcus superior tumors (n = 15).

TABLE 5. Patient Characteristics and Outcome after Induction Therapy for Superior Sulcus and Central T4 Tumors

<table>
<thead>
<tr>
<th>Study</th>
<th>Superior Sulcus</th>
<th>Central T4 (%)</th>
<th>Induction Therapy</th>
<th>Radiographic SD or Response (%)</th>
<th>Surgery (%)</th>
<th>Operative Mortality (%)</th>
<th>R0 Resection (%)</th>
<th>5 yrs Overall (%)</th>
<th>5 yrs R0 Resection (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rendina et al.</td>
<td>57</td>
<td>0</td>
<td>100</td>
<td>Ch</td>
<td>NR</td>
<td>73.8</td>
<td>2.3</td>
<td>63</td>
<td>NR</td>
</tr>
<tr>
<td>Kwong et al.</td>
<td>37</td>
<td>86.5</td>
<td>13.5</td>
<td>Ch + RT (60 Gy)</td>
<td>100</td>
<td>100</td>
<td>2.7</td>
<td>97</td>
<td>50</td>
</tr>
<tr>
<td>20</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>86</td>
<td>80</td>
<td>2.3</td>
<td>76</td>
<td>46</td>
</tr>
<tr>
<td>Rush et al.</td>
<td>110</td>
<td>71</td>
<td>29</td>
<td>Ch + RT (45 Gy)</td>
<td>86.8</td>
<td>76</td>
<td>3.5</td>
<td>68</td>
<td>56</td>
</tr>
<tr>
<td>Kunitoh et al.</td>
<td>76</td>
<td>74</td>
<td>26</td>
<td>Ch + RT (45 Gy)</td>
<td>100</td>
<td>94</td>
<td>6.4</td>
<td>87</td>
<td>46</td>
</tr>
<tr>
<td>Marra et al.</td>
<td>31</td>
<td>81</td>
<td>19</td>
<td>CH CH + RTb</td>
<td>87</td>
<td>84.4</td>
<td>0</td>
<td>78</td>
<td>74</td>
</tr>
<tr>
<td>Present series</td>
<td>32</td>
<td>15.6</td>
<td>31.2</td>
<td>53.1</td>
<td>87</td>
<td>84.4</td>
<td>0</td>
<td>78</td>
<td>74</td>
</tr>
</tbody>
</table>

a C2: 9; cN3: 1; cM1: 5.
b Hyperfractionated radiotherapy.
R0, completely resected patients; NR, not reported; RT, radiotherapy; Ch, chemotherapy.
tumor from adjacent mediastinal nodes. Therefore, invasive because it is often impossible to discriminate on PET scan value of PET scan is much lower in this group of patients with a 5-year survival after lobectomy of 60% compared with patients, we performed an anatomic resection. In patients and could technically be resected by wedge resection. In all to be helpful to reduce the extent of resection of vital covered with a broad pleural flap. 

Superior sulcus tumors, an intercostal muscle flap cannot be used. In these patients, the bronchial stump was posterior chest wall resection in most of the patients with pneumonectomy is more at risk for bronchopleural dehiscence. In patients with centrally located T4 tumors, there is a high chance of pneumonectomy, and pneumonectomy is more at risk for bronchial wound dehiscence. In patients with superior sulcus tumors most resections can be performed with lobectomy. Moreover, due to the posterior chest wall resection in most of the patients with superior sulcus tumors, an intercostal muscle flap cannot easily be used. In these patients, the bronchial stump was covered with a broad pleural flap.

Furthermore, the liberal use of frozen sections proved to be helpful to reduce the extent of resection of vital mediastinal structures. Some superior sulcus tumors are small and could technically be resected by wedge resection. In all patients, we performed an anatomic resection. In patients with superior sulcus tumors, a survival benefit was shown with a 5-year survival after lobectomy of 60% compared with 33% after limited resection. After lobectomy, there was also reduction in local recurrence. In our study, in 74% of resected specimens no or only minimal microscopic vital tumor was found. Long-term results of SWOG trial 9416 showed, however, that minimal microscopic residual disease was not predictive of outcome, this in contrast to outcome of patients with pathologic CR who had a statistically significant better survival. The concurrent chemoradiotherapy scheme with cisplatin-etoposide and radiotherapy (45 Gy) have shown to be effective and safe in trimodality treatment. Newer drugs or increasing the dose of radiation may be more effective but also more toxic. In our study, treatment morbidity was minimal with no mortality and only two patients experienced local recurrence (7.4%). Some centers have either used hyperfractionation or added higher dose three-dimensional radiation with doses varying from 50 to 70 Gy. Complete resection was as high as 97.3% with an operative mortality of 2.7%. The overall median survival time was 2.6 years.

The most common site of metastasis was the brain, which accounted for half of all recurrences in our series and affected 7% of patients. In the Intergroup study, up to 40% of patients had brain metastasis as the only site of recurrence. There is evidence from nonrandomized studies in locally advanced NSCLC that prophylactic paracranial irradiation (PCI) reduces recurrence in the brain and improved survival. Because sulcus superior tumors and centrally located T4 tumors are relatively rare, it is not feasible to perform a randomized PCI trial in this subset of patients. Given the fact that many patients develop brain metastasis as the only site of recurrence, PCI should be considered in patients who had a complete resection after induction chemoradiotherapy.

In our study, clinical T staging was mainly based on CT or MRI imaging techniques. We are aware that this can be subject to a potential margin of error. All these patients were discussed at the multidisciplinary oncological meeting in the presence of an experienced chest radiologist and nuclear physician. Studies have shown that in experienced hands, CT can be often accepted for the diagnosis of central T4 tumors. A possible way to discriminate between cT3 and cT4 might be thoracoscopy that was used in 20 of 57 patients in the study of Rendina et al. or alternatively pericardioscopy. Nevertheless, since it is impossible by thoracoscopy to directly palpate the tissues, it is often difficult to differentiate between real T3 and T4 lesion. Moreover, there is a risk of tumor spread during dissection of the lung and the mediastinal organs.

Our study results give further support to recent published guidelines of the American College of Chest Physicians. In patients with potentially resectable, nonmetastatic sulcus superior tumor, preoperative concurrent chemoradiotherapy before resection is recommended (grade IB). At the present time, there are no guidelines for T4N0–N1 disease. It is unlikely to have a prospective phase 3 study testing the role of surgery in this uncommon subset of patients. Based on our results and other published data, it seems appropriate to propose trimodality treatment to selected fit patients with T4N0–N1 disease.
REFERENCES


