Results of Primary Surgery With T4 Non–Small Cell Lung Cancer During a 25-Year Period in a Single Center: The Benefit is Worth the Risk

Bedrettin Yıldızeli, MD, Philippe G. Dartevelle, MD, Elie Fadel, MD, Sacha Mussot, MD, and Alain Chapelier, MD

Department of Thoracic and Vascular Surgery and Heart-Lung Transplantation, Hôpital Marie-Lannelongue, Paris-Sud University, Le Plessis Robinson, France

Background. The purpose of this study was to assess operative mortality, morbidity, and long-term results of patients with surgically resected T4 non–small cell lung carcinoma.

Methods. A retrospective review of 271 patients with T4 non–small cell lung carcinoma between 1981 and 2006 was undertaken. They were divided into four subgroups: 126 patients with superior sulcus tumors, 92 with carinal involvement, 39 with superior vena cava replacement, and 14 with the tumor invading other mediastinal structures. There were 221 men and 50 women with a mean age of 56.3 years. Resection was complete in 249 (92%) patients. The pathologic N status was N0/N1 in 208 and N2/N3/M1 in 63 patients.

Results. Operative mortality and morbidity rates were 4% and 35%, respectively. Overall 5-year survival rate was 38.4%. It was 36.6% for superior sulcus tumor, 42.5% for carinal involvement, 29.4% for superior vena cava replacement, and 61.2% for mediastinal group. By multivariate analysis, only three factors influenced survival: nodal status (N0/N1 versus N2/3/M1; 43% versus 17.7% at 5 years, respectively; \( p = 0.01 \)), complete resection (R0 versus R1; 40.4% versus 15.9%, respectively; \( p = 0.006 \)), and invasion of the subclavian artery (with versus without invasion; 24.9% versus 41.7%, respectively, \( p = 0.02 \)).

Conclusions. In highly qualified centers, radical surgery of T4 N0/N1 non–small cell lung carcinoma can be performed with a 4% mortality rate and may yield a 43% 5-year survival rate. These results seem to indicate primary surgery as the treatment of choice for T4 non–small cell lung carcinoma, whenever a complete resection is thought to be technically feasible and the patient’s condition is compatible with the extent of the planned surgery.

© 2008 by The Society of Thoracic Surgeons

Lung cancer remains the most fatal cancer worldwide [1], and 10% of patients with lung cancers diagnosed in the European population are alive at 5 years [2]. During the past two decades, surgical techniques for resecting locally advanced tumors have been refined [3–13], allowing the complete resection of the subset of T4 patients. However, fewer series have provided up to 30% to 40% long-term survival data [6, 7, 10]. As induction therapy poses special perioperative risks and technical challenges, the debate continues especially for the patients with T4N0 disease. T4N0 tumors are unlikely to be biologically the same as T1 to T4N3 tumors and, by definition, are tumors with less propensity to metastasize [3].

In this study we retrospectively analyzed the survival of patients with resected T4 non–small cell lung cancer (NSCLC) according to the subgroups of T4 category. The main objective of this study was to determine whether the benefit is worth the risk.

Patients and Methods

Patients

Between 1981 and 2006, 6,097 patients underwent pulmonary resections because of NSCLC. Among them, 271 (4.4%) who underwent resection for pathologic T4 tumors were reviewed. The patients were divided into four subgroups: 126 patients with superior sulcus tumors that were resected through an anterior transclavicular approach, 92 with carinal involvement, 39 with superior vena cava (SVC) invasion requiring graft interposition, and 14 with the tumor invading the SVC.
mediastinum, esophagus, heart, and great vessels. Patients undergoing resection for benign diseases or malignant diseases other than NSCLC and those with presence of malignant pleural or pericardial effusion or with a satellite tumor nodule in the primary tumor lobe were excluded from the study. Data were obtained from the hospital database, hospital charts, referring physicians, and the patients or the patients’ family. Postoperative death included all patients who died within 30 days of surgical intervention or before being discharged from the hospital. Follow-up was complete for all patients. The study was approved by the institutional review board.

Only some specific points regarding our preoperative workup are presented here [7–13]. In addition to the routine investigations, computed tomography or magnetic resonance imaging of the brain is routinely performed. Mediastinoscopy is only performed when chest computed tomography shows mediastinal nodes larger than 1.0 cm in diameter or when positron emission tomography shows mediastinal fixation to exclude N2 disease. Our techniques of extended lung resections have been reviewed in detail elsewhere [6–13].

### Statistical Analysis

All results are expressed as medians and ranges or as absolute numbers and percentages. Statistical significance was evaluated using the \( \chi^2 \) test. Potential risk factors for postoperative mortality were identified by means of univariate and multivariate analysis. All variables were initially subjected to univariate analysis with the \( \chi^2 \) test to avoid overadjustment by using too many variables in the multivariate models. Factors with a probability value of less than 0.05 were then considered as risk factors in the multivariate logistic regression analysis. Survival rates were calculated by means of life-table analysis. Kaplan–Meier curves were plotted and compared with the log-rank test. StatView V (Abacus Concept, Berkeley, CA) software was used for all analyses.

### Results

#### Overall

The characteristics of the 271 patients are summarized in Table 1. There were 221 (81.5%) men with a mean age of 56.3 years. Mediastinoscopy was performed in 37 (13.6%)...
patients. Among 7 patients with synchronized solitary metastasis, 3 had a brain metastasis, 2 had single parietal pleural metastasis, 1 had an adrenal metastasis, and 1 had contralateral lung metastasis. There were no significant differences in sex, age, histologic assessment, or pathologic N status among the four groups. Tumor size ranged between 1 and 17 cm (median, 5 cm).

Among 126 patients with superior sulcus tumor, 28 underwent a combined “en bloc” resection of the first thoracic vertebrae at three or four levels associated with spinal fixation. In the group of SVC, 17 patients required a combined right carinal pneumonectomy. The resection of the esophagus was limited to the muscle wall in 11 patients. Nine operations were performed under cardiopulmonary bypass.

The operative mortality according to the type of procedure is reported in Table 2. Overall 30-day mortality and morbidity rates were 4% (n = 11) and 35% (n = 95), respectively. The median length of hospitalization was 15 days (range, 0 to 120 days). The types of complications are summarized in Table 3. Pulmonary edema and atelectasis were the most common postoperative complications.

Eleven patients (4%) died postoperatively. Six patients died of a bronchopleural fistula on postoperative day 9, 12, 15, 20, 22, and 26. Two patients died of an acute pulmonary edema on postoperative day 7 and 14. One patient died on the 19th postoperative day of acute respiratory distress syndrome, 1 of sepsis on day 13, and 1 of pulmonary embolism on day 14. Among the risk factors that were investigated, those showing a significant effect on the development of postoperative mortality in the multivariate analysis were right pneumonectomy (n = 115/9; p = <0.001; Table 4). Among the 22 patients with R1 resection, 12 had superior sulcus tumor, 6 had SVC replacement, 2 had carinal involvement, and the other 2 had mediastinal invasion.

Follow-up was completed up to August 2007 or to the date of death for 271 patients. The mean observation period after the operation was 44.2 months (range, 0 to 255 months). Among the 271 patients, 86 (31.7%) patients are still alive. The actuarial 5-year survival was 38.4% with 28 months of median survival time (Fig 1). The

![Fig 1. Survival curve of the 271 patients with resected T4 non–small cell lung cancer. Five-year survival was 38.4% and 10-year survival was 26%. Median survival time was 28 months.](image)
Table 3. Postoperative Complications

<table>
<thead>
<tr>
<th>Complications</th>
<th>Superior Sulcus Tumor</th>
<th>Carinal Resection</th>
<th>SVC Reconstruction</th>
<th>Mediastinal Invasion</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Morbidity</td>
<td>Mortality</td>
<td>Morbidity</td>
<td>Mortality</td>
<td>Morbidity</td>
</tr>
<tr>
<td></td>
<td>n %</td>
<td>n %</td>
<td>n %</td>
<td>n %</td>
<td>n %</td>
</tr>
<tr>
<td>Anastomotic complications with or without BPF</td>
<td>3 2.4</td>
<td>... ...</td>
<td>7 7.6</td>
<td>3 3.3</td>
<td>1 2.6</td>
</tr>
<tr>
<td>Pulmonary edema</td>
<td>5 4</td>
<td>... ...</td>
<td>8 8.7</td>
<td>2 2.2</td>
<td>... ...</td>
</tr>
<tr>
<td>Sepsis</td>
<td>4 3.2</td>
<td>... ...</td>
<td>1 1.1</td>
<td>... ...</td>
<td>... ...</td>
</tr>
<tr>
<td>ARDS</td>
<td>5 4</td>
<td>1 0.8</td>
<td>3 3.3</td>
<td>... ...</td>
<td>1 2.6</td>
</tr>
<tr>
<td>Pulmonary emboli</td>
<td>... ...</td>
<td>... ...</td>
<td>2 2.2</td>
<td>1 1.1</td>
<td>... ...</td>
</tr>
<tr>
<td>Atelectasis</td>
<td>10 7.9</td>
<td>... ...</td>
<td>5 5.4</td>
<td>... ...</td>
<td>... ...</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>7 5.6</td>
<td>... ...</td>
<td>5 5.4</td>
<td>... ...</td>
<td>1 2.6</td>
</tr>
<tr>
<td>Hemothorax</td>
<td>6 4.8</td>
<td>... ...</td>
<td>3 3.3</td>
<td>... ...</td>
<td>... ...</td>
</tr>
<tr>
<td>Chylothorax</td>
<td>4 3.2</td>
<td>... ...</td>
<td>3 3.3</td>
<td>... ...</td>
<td>... ...</td>
</tr>
<tr>
<td>SVT</td>
<td>... ...</td>
<td>... ...</td>
<td>3 3.3</td>
<td>... ...</td>
<td>... ...</td>
</tr>
<tr>
<td>Scapula lata</td>
<td>3 2.4</td>
<td>... ...</td>
<td>... ...</td>
<td>... ...</td>
<td>... ...</td>
</tr>
<tr>
<td>Empyema</td>
<td>1 0.8</td>
<td>... ...</td>
<td>1 1.1</td>
<td>... ...</td>
<td>... ...</td>
</tr>
<tr>
<td>Cardiac herniation</td>
<td>1 0.8</td>
<td>... ...</td>
<td>1 1.1</td>
<td>... ...</td>
<td>1 2.6</td>
</tr>
<tr>
<td>CSF leak</td>
<td>1 0.8</td>
<td>... ...</td>
<td>... ...</td>
<td>... ...</td>
<td>... ...</td>
</tr>
<tr>
<td>Skin abscess</td>
<td>... ...</td>
<td>... ...</td>
<td>... ...</td>
<td>... ...</td>
<td>... ...</td>
</tr>
<tr>
<td>Mediastinitis</td>
<td>... ...</td>
<td>... ...</td>
<td>... ...</td>
<td>... ...</td>
<td>... ...</td>
</tr>
<tr>
<td>Total</td>
<td>50 39.7</td>
<td>1 0.8</td>
<td>39 42.4</td>
<td>6 6.5</td>
<td>4 10.3</td>
</tr>
</tbody>
</table>

ARDS = acute respiratory distress syndrome; BPF = bronchopleural fistula; CSF = cerebrospinal fluid; SVC = superior vena cava; SVT = supraventricular tachycardia.
overall 5-year survivals according to the four subgroups within the T4 category were as follows: superior sulcus tumor, 36.6%; carinal involvement, 42.5%; SVC invasion, 29.4%; mediastinal group, 61.2%. There was no significant difference among the four groups (Fig 2).

Factors affecting survival in patients with T4 NSCLS are listed in Table 5. Survival reached 43% at 5 years in patients with N0/N1 disease and was significantly better than in those with N2+ disease (ie, N2 or N3 or M1; survival of 17.7% at 5 years; \( p = 0.002 \); Fig 3). There was no difference in survival at 5 years between patients with N0 or N1 disease (39.6% versus 47.1%, respectively; \( p = 0.4 \)). By multivariate analysis, only three factors significantly and independently influenced survival: nodal status (N0/N1 versus N2/N3/M1; \( p = 0.01 \)), complete resection (R0 versus R1; 40.4% versus 15.9%, respectively; \( p = 0.006 \); Fig 4), and invasion of the subclavian artery (with versus without invasion; 24.9% versus 41.7%, respectively; \( p = 0.02 \); Fig 5).

Recurrences were observed in 138 patients (51%); 29 were at local sites, 94 were at distant sites, and 15 were at both distant and local sites in the remaining patients. One hundred twenty-eight patients with R0 resection had recurrences; 24 patients had a locoregional, 83 had a distant, and 15 had both sites. On the other hand, 16 of 22 patients with incomplete resection had recurrences; 11 patients had a locoregional and 5 had a distant.

**Superior Sulcus Tumors**

Postoperative adjuvant therapy was used in 80 patients. Among the 24 patients who underwent wedge resection, 17 had an adjuvant therapy, either radiochemotherapy (n = 14), chemotherapy (n = 2), or radiotherapy (n = 1). Median survival time was 28 months, and overall 5- and 10-year survivals were 36.6% and 25.9%, respectively. The overall 5-year survival was 38.5% for the patients who had no intervertebral foramina involvement whereas it was 27.2% for the 28 patients who underwent en bloc
resection of the thoracic inlet and intervertebral foramina (p = 0.8). Median survivals were 29 and 25 months, respectively. Survival reached 39.3% at 5 years in patients with R0 resection and was significantly better than in those with R1 resection (survival of 9.5% at 5 years; p = 0.008). Patients with subclavian artery invasion had a survival of 25.4% at 5 years, which is significantly worse than the patients who had no subclavian artery invasion (42.3% at 5 years; p = 0.01). By multivariate analysis, R0 resection and the subclavian artery involvement influenced survival (p = 0.01, each).

**Carinal Resection**

All 9 patients with a tracheal dehiscence had an empyema, and 3 of them died while in the hospital. The patient with local necrosis and one with tracheal dehiscence were treated conservatively. One had an anastomotic stenosis requiring an endotracheal stent later on; 3 patients underwent thoracomyoplasty and 1 had omentoplasty. A total of 10 patients (10.8%) had some degree of pulmonary edema in the immediate postoperative period. Five of them required reintubation, and 2 died. All 6 deaths occurring from tracheal dehiscence or acute respiratory distress syndrome happened after right carinal pneumonectomy.

Median survival time was 28 months, and the actuarial 5-year survival was 42.5% for patients with carinal resection (Fig 2). Survival reached 49.8% at 5 years in patients with N0/N1 disease and was significantly better than in those with N2 disease (survival of 17% at 5 years; p = 0.007). The actuarial 5-year survival was 50% in patients who underwent partial resection of the SVC whereas the 5-year survival was 41.5% for the remaining cohort of patients (p = 0.2). However, survival was 43.5% at 5 years in patients with R0 resection and was significantly better than in those with R1 resection (survival of 0% at 5 years; p = 0.04). By multivariate analysis, only nodal status

---

### Table 5. Factors Affecting Survival in Patients With T4 Non–Small Cell Lung Cancer (n = 271)

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>n</th>
<th>5-Year Survival</th>
<th>p Value Univariate Analysis</th>
<th>p Value Multivariate Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neoadjuvant treatment (Yes/No)</td>
<td>75/196</td>
<td>37.0/38.8</td>
<td>0.7</td>
<td></td>
</tr>
<tr>
<td>Pneumonectomy/lesser resections</td>
<td>134/137</td>
<td>39.2/37.7</td>
<td>0.9</td>
<td></td>
</tr>
<tr>
<td>Subclavian artery involvement (Yes/No)</td>
<td>50/221</td>
<td>24.9/41.7</td>
<td>0.01</td>
<td>0.02</td>
</tr>
<tr>
<td>SVC invasion (Yes/No)</td>
<td>52/220</td>
<td>34.7/39.3</td>
<td>0.9</td>
<td></td>
</tr>
<tr>
<td>Complete resection (R0/R1)</td>
<td>249/22</td>
<td>40.4/15.9</td>
<td>0.005</td>
<td>0.006</td>
</tr>
<tr>
<td>Squamous cell cancer/non–squamous cell cancer</td>
<td>133/138</td>
<td>37.2/37.5</td>
<td>0.8</td>
<td></td>
</tr>
<tr>
<td>N0/N1 versus N2/N3/M1</td>
<td>208 versus 63</td>
<td>43.0 versus 17.7</td>
<td>0.002</td>
<td>0.01</td>
</tr>
<tr>
<td>Adjuvant treatment (Yes/No)</td>
<td>139/132</td>
<td>34.7/42.4</td>
<td>0.8</td>
<td></td>
</tr>
</tbody>
</table>

SVC = superior vena cava.

---

Fig 3. Survival curves of patients with pathologic N0/N1 (heavy line; n = 208) and N2/N3 and M1 (thin line; n = 63) status (p = 0.003). Five-year survival was 43% for N0/N1 patients and 17.7% for N2+ patients; median survival time was 33 months for N0/N1 patients and 20 months for N2+ patients.

Fig 4. Survival curves of patients with complete (heavy line; n = 249) and incomplete (thin line; n = 22) resection (p = 0.01). Five-year survival was 40.4% for complete resection and 15.9% for incomplete resection; median survival time was 32 months for complete and 14 months for incomplete resection.
Tumors invading the mediastinum were found.

Specific factors affecting survival in patients with mediastinal invasion were observed. Median survival time was 20 months and 31 months, respectively. Actuarial 5-year survival was 61.2% (Fig 2). No significant and independently influenced survival (N0/N1 versus N2+; \( p = 0.04 \)).

Superior Vena Caval Resection With Superior Vena Caval Replacement

Median survival time was 19 months, and the actuarial 5- and 10-year survival rates were 29.4% and 22.1%, respectively. However, survival reached 37.5% at 5 years in patients with N0/N1 disease and was not significantly better than in those with N2+ disease (survival of 19.6% at 5 years; \( p = 0.1 \)). The actuarial 5-year survival was 13.1% with a median of 46 months in patients who underwent a carinal pneumonectomy and replacement of the SVC whereas the 5-year survival was 43.2% with a median of 19 month for the patients who had no carinal involvement (\( p = 0.02 \)). Survival was 51% at 5 years in patients with non–squamous cell carcinoma and was significantly better than in those with squamous cell carcinoma (12.1% at 5 years; \( p = 0.06 \)). By multivariate analysis, carinal involvement and non–squamous cell cancer significantly and independently influenced survival (\( p = 0.01 \) and 0.02, respectively).

Resection of Non–Small Cell Lung Carcinoma Invading the Mediastinum

The actuarial 5-year survival was 61.2% (Fig 2). No specific factor affecting survival in patients with mediastinal invasion was found.

Comment

Despite subsequent revisions, the international staging systems (American Joint Committee on Cancer [AJCC], International Union Against Cancer [UICC]) still categorize stage IIIB NSCLC as an unresectable disease with a dismal prognosis of about 7% [14]. However, there may be a different biologic behavior in patients with local T4 disease and those with N2M3 nodal diseases or pleural effusions within the stage classification. In this study the patients with resected T4 NSCLC belonged to four heterogeneous subgroups according to their survival analyses. The factors that were found to possibly affect survival were the completeness of resection, the lymph node status, and the subclavian artery involvement. Of course, variations exist in the surgical results for patients with tumor invading the adjacent organs.

The overall 5-year survival rates after combined radio-surgical treatment of superior sulcus tumors attributable to NSCLC range from 18% to 56% [15–17]. Recently long-term results of the Southwest Oncology Group trial 9416 have been published [18]. One hundred ten patients with superior sulcus tumors received induction chemoradiotherapy, and 88 of them subsequently underwent thoracotomy. Given a 30% complete pathologic response and a 44% 5-year survival, the authors concluded that local control and overall survival seem markedly improved relative to previous studies of radiation plus resection. In our study, overall 5-year survival was found to be 36.6% for the patients with superior sulcus tumors, and the long-term survival was affected by both complete resection and subclavian artery invasion. On the other hand, invasion of the intervertebral foramina, induction chemotherapy, and adjuvant therapies did not affect the survival of the patients with superior sulcus tumors. It is obvious that the main factor affecting the long-term survival is complete resection along with negative mediastinal lymph node involvement. Our nearly 91% rate of complete resection is acceptable, and the main difficulty was observed in patients with intervertebral foramina involvement. A multidisciplinary team is essential for the patients presenting with vertebral invasion [9]. Regarding this fact, we agree with the recent American College of Chest Physicians evidence-based clinical practice guidelines [19] that in patients with a Pancoast tumor involving the subclavian vessels or vertebral column, resection should be undertaken only at a specialized center to achieve a complete resection. On the other hand, we do not agree with the recommendation that patients with a potentially resectable, nonmetastatic Pancoast tumor are to be given preoperative concurrent chemoradiotherapy. Induction chemotherapy did not seem to increase completeness of the resection, and its toxic effects prevents up to 20% of the patients who are potentially candidates for thoracotomy from undergoing the procedure [18]. In addition, it has been reported that an extended resection after induction therapy results in higher rates of mortality and morbidity compared with those after a standard resection [20–22]. Therefore, we think induction therapy should be considered for the patients with mediastinal lymph node involvement. The high risk of brain relapse seen in a phase II trial [18] was similar to our observations. In the present study, 50 patients with a Pancoast tumor died of distant tumor recurrence. This raised the issue of whether patients...
should be considered for prophylactic cranial radiotherapy [23]. Randomized trials are ongoing to answer this question [23].

Recent series have shown that carinal resection is relatively safe in experienced centers and can be associated with good long-term survival in selected patients [7, 19, 24–26]. Our overall operative mortality of 6.5% with the median 5-year survival of 42.5% compares favorably with that seen in other recent series [19]. These results are considerably better than those from earlier reported series and likely account for the improvement in surgical and anesthetic techniques. Patients who underwent complete resection with N0/N1 diseases showed better survival than those with R1 resection and N2+ diseases. As patients with positive mediastinal lymph node metastases have a dismal prognosis, N2 disease should be considered a contraindication to carinal resection [7]. Induction therapy seems to improve survival if the mediastinal nodes can be sterilized before the lung resection. However, induction therapy could potentially be associated with increased operative morbidity and mortality in patients requiring right carinal pneumonectomy. Recently, it has been reported that operative mortality increased from 6.7% to 13% after induction therapy in patients undergoing right carinal pneumonectomy [7]. Martin and associates [27] also reported an operative mortality as high as 24% with right pneumonectomy after induction therapy. Considering the results of recent trials on adjuvant chemotherapy for patients with completely resected NSCLC, we now recommend postoperative chemotherapy for most patients undergoing carinal resection for NSCLC, regardless of the nodal status [28, 29]. However, we consider adjuvant radiation therapy only in patients with positive resection margin, or N2 disease and extracapsular extension.

Although there are scattered reports of long-term survivors from extended resections of lung cancers involving the superior vena cava, aorta, left atrium, main pulmonary artery, or esophagus, there are fewer solid data to support these extended operations. It has been well accepted that very selected patients with mediastinal invasion along with SVC invasion but without mediastinal node involvement can be viewed as candidates for surgery [19].

Spaggiari and colleagues [29] analyzed 109 patients who underwent SVC resection and found that mortality rate was 12% and 5-year survival was 21%. Patients who had an induction treatment presented with an increased risk of major complications. Suzuki and associates [30] and Shargall and coworkers [31] reported a total of 55 patients with 12% of mortality rate and 24% with a 5-year survival. It has been reported that a total of 189 patients who were operated on for SVC invasion had a mortality rate of 12% with a median 25% 5-year survival [19].

These operations need complex resections and reconstructions, and may also need use of cardiopulmonary bypass. Our 1.1% and 0.3% mortality rates for the SVC and mediastinal groups, respectively, support the recommendation of the American College of Chest Physicians [19] that resection is to be undertaken only at a specialized center. In the present study, morbidity and mortality were linked with the association of a carinal pneumonectomy. We found that carinal involvement significantly affected 5-year survival. Therefore, patients who may undergo a right carinal pneumonectomy with SVC resection and replacement should be examined more carefully to assess the risk and the benefit of the operation.

Surgical reports dealing with tumors invading the pulmonary artery trunk are limited [32, 33]. Because all patients died within 30 months from operation, invasion of the pulmonary artery trunk was considered technically resectable but incurable biologically.

Systemic arterial (aorta) and esophageal invasion of T4 lung cancer carry the poorest long-term outcomes [3, 19]. Vascular resection and reconstruction of the aorta and left atrium have been safely described with 5-year survival rates of 20%. Combined pulmonary and aorta resection is described with 5-year survival rates of 31% [34]. Combined pulmonary and left atrial resection has been described most recently with 5-year survival rates of 10% [35]. Recently, Ohta and colleagues [36] reported that 16 patients underwent thoracic aorta resection along with a lung resection with a mortality rate 12.5% and 5-year survival rates of 70% for patients with N0 disease and 16.7% for patients with N2 or N3 disease.

We used cardiopulmonary bypass for 9 patients with 0% mortality. The use of cardiopulmonary bypass does not appear to increase the risk of cancer dissemination. Several series have reported combining lung resection for bronchogenic carcinoma with aorto coronary bypass surgery during the same operative procedure with good early and long-term results despite the use of cardiopulmonary bypass [13].

Long-term outcome of patients with locally advanced lung cancer depends primarily of completeness of resection. Martini and associates [37] have reported a series of lung cancer invading the mediastinum, and observed that the 5-year survival rate was 30% if the tumor was completely resected, whereas it was only 14% if it was incompletely resected. Similar observations were reported by Shiraiishi and colleagues [38] in a series of lung cancer invading the thoracic aorta with a 5-year survival rate of 36.5% if the tumor was completely resected.

Another important issue is mediastinal staging of patients with T4 NSCLC. Because this study covers a period of 25 years, only 13.6% of our patients underwent mediastinoscopy, and unfortunately we have found that 20.7% of the patients had either N2 or N3 disease. This figure really shows the importance of preoperative mediastinal staging to select the proper patients who may benefit from a long-term survival after surgery. If a lymph node is 1 cm or less on a transverse computed tomographic scan image, we also accept this lymph node as a normal-sized mediastinal lymph node. On the other hand, newer-generation integrated positron emission tomography–computed tomography imagers also help us perform more accurate staging of the mediastinum. Therefore, as a modern approach we also started to perform positron
emission tomography scanning for mediastinal and extrathoracic staging. If an abnormal result on fluorodeoxyglucose–positron emission tomography scan is obtained, we do perform mediastinoscopy. However, other methods of invasive mediastinal staging like esophageal ultrasound with needle aspiration, transbronchial needle aspiration, endobronchial ultrasound with needle aspiration, and transthoracic needle aspiration are also available to stage the mediastinum. We recommend performing mediastinoscopy at the time of the planned carinal resection to avoid the development of scaring tissue along the trachea and to take advantage of the tracheal mobilization to reduce tension at the anastomotic site.

It is difficult to have a conclusion from our results for the patients with mediastinal invasion owing to the limited number. However, we agree that these patients need complex resections and reconstructions, and therefore they should be very carefully selected before surgical resection is undertaken because of the limited survival and the high mortality [19].

There are, however, some limitations of this study. First, it would be better to provide data about the disease-free survival instead of the overall survival. However, because of the retrospective nature of the study, we had no chance to get more accurate information regarding the disease-free survival. Second, T4 NSCLC poses a formidable therapeutic challenge because of the proximity to several vital structures in the body. Although it is difficult to perform a randomized study regarding induction therapy versus surgery as a first-line treatment for patients with T4N0 or N1 disease, future studies are needed to address the continuing difficulties of systemic relapse after surgery.

In conclusion, patients with locally advanced NSCLC should be treated with aggressive multidisciplinary therapy in a manner that maximizes the chance for long-term cure while minimizing the overall risks of treatment as pointed out in the American College of Chest Physicians evidence-based clinical practice guidelines [39]. Advances in the perioperative management and postoperative care, along with a careful patient selection, will likely make the operative mortality and morbidity less prohibitive and yield a more favorable prognosis. It has been well demonstrated that the prognosis after operations for T4 tumors mainly depends on the N stage and complete resection. Patients with N0 or minimal N1 disease and patients with complete resection do significantly better after radical resection, a finding that clearly justifies operative therapy in these patients. Presence of pN2 disease should be considered a potential contraindication to resection of T4 tumors. On the other hand, both the technical complexity of the operation and its rare occurrence therefore suggest centralization of the procedure to departments that express profound and continuous interest in such problems and that at the same time have a high degree of experience with general thoracic, cardiac, vascular, and spinal procedures. Our policy regarding locally advanced lung cancer patients is to perform surgery on first intention, whenever a complete resection is thought to be technically possible. Complete resection of T4 NSCLC results in a 40.4% 5-year survival rate. Patients with NSCLC who have carinal involvement, SVC invasion, and superior sulcus tumor even with vertebral invasion or mediastinal invasion without mediastinal lymph node involvement should undergo radical surgery without any attempt of giving neoadjuvant chemotherapy.

The thoracic medical and surgical community should promote all efforts to extend the surgical indications for locally advanced NSCLC, making these operations available whenever possible to patients in whom radical resection can be achieved.

References

18. Rusch VW, Giroux DJ, Kraut MJ, et al. Induction chemoradia-

tion and surgical resection for superior sulcus non–small-

cell lung carcinomas: long-term results of Southwest Oncol-

gy Group Trial 9416 (Intergroup Trial 0160). J Clin Oncol
19. Shen RK, Meyers BF, Larner JM, Jones DR. Special treatment
issues in lung cancer: ACCP evidence-based clinical practice
20. Matsubara Y, Takeda S, Mashimo T. Risk stratification for
lung cancer surgery: impact of induction therapy and ex-
apy increases perioperative complications in patients under-
going resection for non–small cell lung cancer. Ann Thorac
complications after combined neoadjuvant treatment of lung
2006;7:1005.
tumors with carinal involvement: technical aspects, results,
25. Mitchell JD, Mathisen DJ, Wright CD, et al. Clinical experi-
117:39–53.
tions of carinal resection for non–small-cell lung cancer. Ann
27. Martin J, Ginsberg RJ, Abolhoda A, et al. Morbidity and
mortality after neoadjuvant therapy for lung cancer: the risks
cisplatin versus observation in resected non–small-cell lung
cava resection with prosthetic replacement for non–small

tion of superior vena cava for lung carcinoma: prognostic
significance of patterns of superior vena cava invasion. Ann
31. Shargall Y, de Perrot M, Keshavjee S, et al. 15 years single
center experience with surgical resection of the superior
vena cava for non–small cell lung cancer. Lung Cancer
2004;45:57–63.
pulmonary artery in patients with lung cancer. Ann Thorac
33. Tsujiya R, Asamura H, Kondo H, Goya T, Naruke T.
Extended resection of the left atrium, great vessels, or both
34. Fukuse T, Wada H, Hitomi S. Extended operations for
non–small cell lung cancers invading great vessels and left
35. Bobbio A, Carbogno P, Grapeggia M, et al. Surgical out-
come of combined pulmonary and atrial resection for lung
lung cancer with infiltration of the thoracic aorta. J Thorac
37. Martini N, Yellin A, Ginsberg RJ, et al. Management of
non–small cell lung cancer with direct mediastinal involve-
38. Shiraishi T, Shirakusa T, Miyoshi T, et al. Extended resection
of T4 lung cancer with invasion of the aorta: is it justified?
39. Jett JR, Schild SE, Ketel RL, Kesler KA. Treatment of non-
small cell lung cancer, stage IIIB. ACCP evidence-based
2665–76.

DISCUSSION

DR PHILIP A. LINDEN (Cleveland, OH): Those are very im-
pressive results. It seems like most of your resections are T4
involving Pancoast or vascular structures. I’m curious how your
patients with esophageal involvement did and what your oper-
atation was, and do you advocate resection for T4 involving the
mediastinum and not vascular structures?

DR DARTEVELLE: For tumors involving the esophagus, it was
a major invasion of the muscular part without invasion of the
mucosa. We didn’t resect the esophagus totally but only the
muscular wall. For mediastinal structures, in 3 cases there was a
direct invasion of the main pulmonary artery bifurcation. Cur-
ously, these 3 patients, whose tumor was resected under bypass,
are still alive a long time after surgery. There were 2 other
patients with aortic arch resection and left subclavian artery
resection. One of them is still alive a long time after surgery.
What was your question about this group?

DR LINDEN: T4 tumors invading the mediastinum historically
have a poor prognosis. I think Memorial Sloan-Kettering in a
paper 15 or 20 years ago, I think by Burt, described a 5-year
survival of 7% or 8%. Do you advocate surgery for T4 tumors not
involving just vascular structures but also invading the medias-
tinum and esophagus?

DR DARTEVELLE: Yes, but I didn’t include the patients with
mediastinal invasion without resection of vascular structures
because I’m not sure it’s truly T4 tumors. I wanted to only study
the patients with major invasions as T4 tumors.

DR FRANK D. DETTERBECK (New Haven, CT): How did you
define an incomplete resection? Did that include a highest
mediastinal node that was positive or did that include only
microscopically positive margins?

DR DARTEVELLE: Incomplete resection is defined by persist-
tent tumor on the margins after resection.

DR DOUGLAS E. WOOD (Seattle, WA): Philippe, I congratulate
you for again showing that you’re the master of T4 disease that
we all aspire to. I think you have emphasized a point that many
of us as surgeons know but many of our medical colleagues do
not; that is, a likely very different biologic behavior of T4N0
disease as evidenced by regional nodal disease. These have
different implications although both are stage IIIB cancer. I think
your series is the only one that shows anything other than 0%
survival for anybody that has T4N2 disease. I personally use N2
disease as an absolute contraindication to operating on these
people. Are you now using nodal status to exclude N2 patients
and are you looking at that more vigorously?
disease, I know that the American philosophy is to not operate on the patients with N2 disease, and at every meeting everyone speaks of N2 disease. I do not have exactly the same philosophy for N2 disease. For N2 disease, when surgery is simple as a lobectomy, I think we can do resection for N2 disease. If it’s a major surgery with a higher risk, for example, a right pneumonectomy or right carinal pneumonectomy, I don’t operate on patients with N2 disease.

DR JOSEPH B. SHRAGER (Philadelphia, PA): I want to start by personally thanking Dr Dartevelle for curing my French uncle by doing an extensive sleeve resection on him—reattaching the right lower lobe to the carina in a gentleman with severe emphysema—about 5 years ago. He has been cured of this disease, and I think he had N2 disease as well.

To just comment on this particular paper, it is important for us all to realize that most papers that report survival after T4 are including tumors with satellite lesions in the same lobe. In the new staging system coming out this year, those are not even going to be classified as T4 anymore. Here, you’re not even including those tumors and you still have a survival of 43%, which I think is really remarkable. So even taking out the best actors in this T4 group from your analysis, you still have these remarkable results.

DR DARTEVELLE: Yes. It’s not the same thing.