

# The Outcome of Surgery and Prognostic Factors in Patients with T4 Non-Small Cell Lung Cancer

## T4 Küçük Hücre Dışı Akciğer Kanseri Hastalarda Cerrahinin Sonuçları ve Prognostik Faktörler

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**ABSTRACT Objective:** We examined the outcome of resection in patients with T4 non-small cell lung cancer (NSCLC) and analyzed the results in various groups established according to organ involvement. Our objective was to distinguish those T4 NSCLC subgroups that would benefit from surgical resection. **Material and Methods:** The records of patients with T4 lung cancer who underwent surgery in our clinic between May 1998 and May 2008 were evaluated retrospectively. Thirty-three patients with T4 NSCLC were enrolled. Classification of T4 tumors were classified according to mediastinal organ invasion, such as the vertebra, carina and major blood vessels. Complete and incomplete resections were compared for survival rates. Kaplan-Meier and log-rank analysis were used for statistical evaluation. **Results:** There were seven cases in the Carinal Invasion Group (CIG), nine in the Vertebral Invasion Group (VeIG) and 13 in the Vascular Invasion Group (VaIG). The remaining four cases were not included in any group and were assessed independently. Overall five-year survival rates were 28.5%, 11.1% and 34.1% in the CIG, VeIG and VaIG, respectively. Median survival times in the CIG, VeIG and VaIG groups were 9, 9 and 12 months, respectively. The prognosis of patients who underwent incomplete resection (five years survival rate= 0%) was worse than that of those who had complete resection (five years survival rate= 34.9%, p= 0.014). **Conclusions:** There was no statistically significant prognostic difference between the groups in terms of mediastinal organ invasion. Extended resection carries a high risk of morbidity and mortality. Surgery should be attempted and a better prognosis can be expected in selected patients, especially if complete resection is performed.

**Key Words:** Carcinoma, non-small cell lung; survival analysis

**ÖZET Amaç:** Bu çalışmada, T4 küçük hücre dışı akciğer kanserli (KHDAK) hastalarda uygulanan rezeksiyon sonuçlarını, T4 tümörün invaze olduğu mediastinal organ grubuna göre analiz ettik. Amacımız cerrahi rezeksiyondan fayda görebilecek olan T4 KHDAK subgruplarını tanımlamaktır. **Gereç ve Yöntemler:** Kliniğimizde Mayıs 1998-Mayıs 2008 tarihleri arasında rezeksiyon uygulanmış olan 33 T4 KHDAK hastasının kayıtları geriye dönük olarak incelendi. Bu olgular T4 kategorisinde invaze edilen mediastinal organa (karina, vertebra, büyük damarlar) göre sınıflandırıldı. Tam ve kısmi rezeksiyonlar sağkalım oranlarına göre karşılaştırıldı. İstatistiksel analiz için Kaplan-Meier ve log rank test kullanıldı. **Bulgular:** Karina invazyonu grubunda (KİG) 7, vertebra invazyonu grubunda (VeİG) 9 ve büyük damar invazyonu grubunda (VaİG) 13 hasta saptandı. Kalan 4 hasta gruplara dahil edilmedi ve ayrı olarak değerlendirildi. T4 kategorisindeki subgruplara göre genel 5 yıllık yaşam süreleri CİG, VeİG ve VaİG'de sırasıyla %28.5, %11.1 ve %34.1 idi. Ortanca yaşam süresi CİG, VeİG ve VaİG'de sırasıyla 9, 9 ve 12 aydı. Kısmi rezeksiyon yapılan olguların prognozu (beş yıllık yaşam süresi %0), tam rezeksiyon yapılanlardan (beş yıllık yaşam süresi %34.9, p= 0,014) daha kötüydü. **Sonuç:** Mediastinal organ tutulumuna göre yaptığımız değerlendirmede, gruplar arasında istatistiksel olarak belirgin prognostik farklılık saptamadık. Bu tümörlerde yapılan genişletilmiş rezeksiyonlar yüksek morbidite ve mortalite riski taşır. Ancak seçilmiş hastalarda, özellikle tam rezeksiyon yapılanlarda daha iyi prognoz beklenebilir.

**Anahtar Kelimeler:** Küçük hücre dışı akciğer karsinomu, sağkalım analizi

**T**<sup>4</sup> primary bronchogenic tumors are locally advanced cancers and have a number of subgroups. According to TNM staging by Mountain, T4 tumors are defined as those of any size but which invade any mediastinal organ such as the heart, great vessels, trachea, esophagus, vertebral body or carina; tumors with malignant pleural or pericardial effusion or those with satellite nodule(s) in the same lobe together with the primary tumor.<sup>1</sup> In patients with T4 tumors, complete resection is not always possible because of the invasion of the mediastinal organs. Morbidity and mortality are high since patients generally require complex extended resections.<sup>2</sup> Considering the low survival rates reported,<sup>3</sup> it is clear why there is a debate on the surgical management of T4 tumors. However, complete resection performed in selected patients delivers a longer survival than all other treatments.

In the present study, we examined the results of resection in patients with T4 non-small cell lung cancer (NSCLC). We evaluated the results in the groups in terms of the invaded organ and performed survival analysis according to the presence of lymph node involvement. Our objective was to distinguish the T4 NSCLC subgroups that would benefit from surgical resection.

## MATERIAL AND METHODS

Thirty-three patients with a pathological diagnosis of T4 NSCLC between May 1998 and May 2008, who underwent extended pulmonary resection, were enrolled. Oral and written informed consents were obtained from all patients. The cases were divided into three subgroups according to the involvement of mediastinal organs. The carina was invaded in seven cases that were classified as the "Carinal Invasion Group (CIG)". Nine cases with vertebral body invasion were included in the "Vertebral Invasion Group (VeIG)" and thirteen cases with great vessel involvement comprised the "Vascular Invasion Group (VaIG)". The pulmonary artery was invaded in five cases in the VaIG, the pulmonary vein in three cases, the superior vena cava in two cases, the aorta in one case, and the left atrium in two cases.

The remaining four cases (three cases, each with a satellite nodule in the same lobe, and one case with malignant pleural effusion determined perioperatively) were not included in any group and were assessed independently.

All patients underwent routine blood tests, thoracic computed tomography (CT) scanning, abdominal ultrasound examination, bronchoscopy, pulmonary function tests, and arterial blood gas analyses before surgery. Cardiac evaluation was carried out when necessary. Cranial CT, magnetic resonance imaging (MRI) or radionuclide bone scans were performed when a metastasis was suspected clinically. Positron emission tomography (PET)-CT scanning became available in our department in 2005 and all cases after that date underwent PET-CT imaging. Before PET-CT, mediastinoscopy was carried out in patients with mediastinal lymph node(s)  $\geq 1$  cm in size in the short axis in thoracic CT scan. After 2005, mediastinoscopy was performed when meaningful <sup>18</sup>F]-2-fluoro-2-deoxy-D-glucose (FDG) uptake was seen in the lymph node(s) in PET-CT scan.

Complete mediastinal lymph node dissection was performed with complete removal of levels 2, 4, 7, 8 and 9. Aortic and subaortic lymph nodes were dissected completely for left-sided tumors. N1 nodes were also dissected completely, as appropriate for the primary surgical procedure performed.

Neoadjuvant therapy was administered before surgery to selected patients with mediastinal lymph node involvement. These cases were reevaluated with mediastinoscopy after neoadjuvant therapy had ended. Those patients who had no sign of N2 disease in the repeat mediastinoscopy underwent resection.

Complete resection was considered successful when the tumor was totally excised and the margin of resection was histopathologically clean. Postoperatively, patients were administered adjuvant therapy if they were able to tolerate this.

Follow-up was continued until May 2008 for 11 patients and until the time of death for 22 patients. The Kaplan-Meier estimator tool was used for

survival analysis. Comparisons between actuarial curves and prognostic factors analysis were made using the log rank test. A p value less than 0.05 was considered statistically significant.

## RESULTS

### PATIENTS

Of the 33 T4 NSCLC cases, 32 were male and one female. Mean age was 58.5 years (40-73 years). Primary tumor was in the right upper lobe in 12 cases, the right lower lobe in 3, the left upper lobe in 4, the left lower lobe in 2, the right middle lobe in 1 and the main bronchus in 11. Five cases had median sternotomy, while the others had posterolateral thoracotomy. Lobectomy was performed in 11 cases, bi-lobectomy in 1 case and pneumonectomy in 21 cases. In the CIG, pneumonectomy was performed via trans-carinal sleeve resection in all cases but one. In thirteen cases, resection was carried out intrapericardially. Twelve of these 13 cases were from the VaIG. In two cases, the superior vena cava was resected tangentially and was repaired primarily for the involvement of a vascular segment approximately 1 cm long. In another patient with aortic involvement, a 7 cm segment of the descending aorta was resected and dacron graft interposition was performed without cardiopulmonary by-pass. In two patients who underwent left atrial resection, the defect was repaired primarily using vascular clamps. In ten cases, including all nine patients from the VeIG, resection of the thoracic wall was carried out in addition to resection of the tumor. The vertebral body was partially excised using a "rongeur" in the VeIG.

Complete resection was performed in 24 (72.7%) cases, while 9 (27.2%) cases underwent incomplete resection. One case in the CIG, five cases in the VeIG, two cases in the VaIG and the case with pleural involvement underwent incomplete resection.

There were 9 cases of adenocarcinoma, 22 cases of epidermoid carcinoma and 2 cases of large cell carcinoma. Lymph node involvement was not determined in 18 cases, while 12 cases were N1 and three cases were N2, histopathologically (Table 1).

**TABLE 1:** Demographic and characteristic data of cases.

Characteristics	T4 category subgroups <sup>a</sup>			
	All (n= 33)	CIG (n= 7)	VeIG (n= 9)	VaIG (n= 13)
<b>Age (years)</b>				
Mean	58.5	55.7	57.3	60
Range	40-73	40-63	44-68	46-72
<b>Sex</b>				
Male	32	6	9	13
Female	1	1	-	-
<b>Histology</b>				
Epidermoid carcinoma	22	6	3	11
Adenocarcinoma	9	-	5	2
Large cell carcinoma	2	1	1	-
<b>Pathological N status</b>				
N0	18	6	8	1
N1	12	1	-	10
N2	3	-	1	2
<b>Localization</b>				
Upper lobe	16	5	9	1
Lower lobe	5	2	-	1
Hilum	11	-	-	10
Middle lobe	1	-	-	1
<b>Resection type</b>				
Complete	24	6	4	11
Incomplete	9	1	5	2

<sup>a</sup> One case with pleural involvement and three cases with satellite nodule were not included in the subgroups.

CIG: Carinal Invasion Group, VeIG: Vertebral Invasion Group, VaIG: Vascular Invasion Group.

In the preoperative period, neoadjuvant therapy was administered to four patients, two of which had N2 disease determined by mediastinoscopy. These two patients were operated after repeat mediastinoscopy revealing that N2 disease had disappeared following neoadjuvant therapy. In the postoperative period, one of these cases was determined to be N1 and the other N0 histopathologically.

The remaining two cases to which neoadjuvant therapy was administered were those in whom we thought it would be difficult to achieve a clean margin of resection during preoperative assessment. One of these patients with right trans-carinal sleeve pneumonectomy developed bronchopleural fistula (BPF) and underwent re-thoracotomy on the fifth day postoperatively. The fistula

was repaired primarily and the anastomosis line was reinforced by means of intercostal muscle flap. The fistula persisted in this patient, and histopathological examination of the bronchoscopic biopsy material revealed the presence of cancer tissue at the line of anastomosis.

**MORBIDITY AND MORTALITY**

Postoperative complications were observed in 12 (36.3%) cases. In two cases, there was hemorrhagia that required re-thoracotomy. Two cases had bronchopleural fistula and three cases had post-pneumonectomy empyema without BPF (Table 2). Hospital mortality (postoperative first 30 days) occurred in 2 (6%) patients, one of whom died of renal and the other of cardiac causes. Two patients died in the second month postoperatively. One of them had metabolic disorders after tracheal sleeve pneumonectomy and the other had BPF and empyema after right upper lobectomy plus chest wall and vertebral resection with instrumentation. During follow-up, mortality from various causes occurred in 20 cases at various times (Table 3). Mortality was due to local recurrence in nine cases and distant metastasis (brain) in two cases. Seven cases died from cardiac and metabolic causes, while the cause of death could not be determined in the remaining two cases.

**SURVIVAL**

The mean postoperative follow-up time was 16.3 months (1-80 months), mean survival time was

26.7 months and the mean five years survival rate was 25.3% (Figure 1). Overall five years survival rates among the CIG, VeIG and VaIG subgroups were 28.5%, 11.1% and 34.1%, respectively and there was no significant difference between the groups (p= 0.58) (Figure 2). Median survival times in the CIG, VeIG and VaIG groups were 9, 9 and 12 months, respectively. Survival analysis according to the localization of the primary tumor (upper lobe, lower lobe and the main bronchus), cell type and pathological N status (N0 versus N1 and N2) revealed no statistically significant difference (p> 0.05) (Table 4, Figure 3).

The prognosis of patients who underwent incomplete resection (five years survival rate: 0%) was worse than that of those who underwent complete resection (five years survival rate 34.9%, p= 0.014) (Figure 4).

**DISCUSSION**

The prognosis of T4 tumors is generally poor. Even though the outcome of surgical treatment is far from satisfactory, stage 3B patients should not be refused for surgery. Longer survival can be expected if complete resection is carried out.<sup>4-7</sup> In T4 tumors, complete resection is not always possible due to the localization of the tumor and the invasion of neighboring organs. The level of complete resection in our study was 72.7%. This is compatible with the levels of 86% and 71% reported by Doddoli et al.<sup>7</sup> and Takahashi et al,<sup>8</sup> respectively. In the present study, the five years survival rate after complete resection (34.9%) was better than that obtained with incomplete resection (0%) (p= 0.014). Five years survival rates after complete and incomplete resections were respectively determined as 46.2% and 10.9% by Pitz et al (p< 0.05), and 29.8% and 0% by Osaki et al (p= 0.0001).<sup>5,9</sup>

Prognosis in T4 tumors varies depending on the invaded organ. The most extensive surgical experience is obtained from cases with carina involvement. Watanabe et al reported a five years survival rate of 22% in a study of 25 carinal resections.<sup>4</sup> Mitchell et al, on the other hand, carried out carina resection in 60 cases and determined a five

**TABLE 2:** Complications and disturbances by T4 subgroups.

Complications	n	T4 subgroups
Expansion difficulty	1	VeIG
Blood reaction + acute renal failure <sup>a</sup>	1	ValG
BPF <sup>b</sup>	2	ValG
Right heart failure <sup>a</sup>	1	VeIG
Bleeding required re-thoracotomy	2	VeIG, ValG
Peripheral arterial embolus	1	ValG
Post-pneumonectomy empyema	3	CIG, ValG
Prolonged air leak	1	VeIG

<sup>a</sup> Hospital mortality,

<sup>b</sup> Broncho-pleural fistula.

CIG: Carinal Invasion Group, VeIG: Vertebral Invasion Group, ValG: Vascular Invasion Group.

**TABLE 3:** Characteristics and survival of patients in the mediastinal group by invaded organ.

Patients (Age, Sex)	T4 location	Histopathology	N status	Follow-up (month)	Status	Recurrence	C/I Resection
47, male	V	Adeno Carcinoma	N0	6	Died	Local	R1
70, male	A	Epidermoid Carcinoma	N1	1	Died		R0
46, male	PA	Epidermoid Carcinoma	N1	5	Died	Local	R1
60, male	C	Epidermoid Carcinoma	N0	2	Died		R1
68, male	V	Epidermoid Carcinoma	N0	1	Died		R0
72, male	PV	Epidermoid Carcinoma	N2	1	Died		R0
44, male	V	Adeno Carcinoma	N0	9	Died	Local	R1
68, male	V	Adeno Carcinoma	N2	17	Died	Local	R0
40, male	C	Epidermoid Carcinoma	N0	80	Alive		R0
57, male	V	Large cell Carcinoma	N0	7	Died	Distant	R1
63, male	C	Epidermoid Carcinoma	N0	76	Alive		R0
63, Female	C	Large cell Carcinoma	N1a	9	Died		R0
50, male	C	Epidermoid Carcinoma	N0	23	Died	Local	R0
53, male	SVC	Epidermoid Carcinoma	N0a	58	Alive		R0
70, male	SVC	Epidermoid Carcinoma	N1	54	Alive		R0
58, male	S	Adeno Carcinoma	N0	8	Died	Distant	R0
63, male	V	Adeno Carcinoma	N0	12	Died		R1
65, male	V	Epidermoid Carcinoma	N0	15	Died		R0
73, male	P	Adeno Carcinoma	N0	32	Alive		R1
53, male	C	Epidermoid Carcinoma	N0	1	Died		R0
63, male	Ao	Epidermoid Carcinoma	N2	3	Died	Local	R0
53, male	A	Epidermoid Carcinoma	N1 <sup>a</sup>	15	Died		R1
61, male	C	Epidermoid Carcinoma	N0 <sup>a</sup>	4	Died	Local	R0
66, male	PA	Adeno Carcinoma	N1	12	Died	Local	R0
56, male	S	Epidermoid Carcinoma	N1	10	Died	Local	R0
56, male	PV	Epidermoid Carcinoma	N1	18	Alive		R0
45, male	V	Adeno Carcinoma	N0	17	Alive		R0
53, male	PA	Epidermoid Carcinoma	N1	11	Died		R0
58, male	S	Epidermoid Carcinoma	N0	11	Alive		R0
64, male	PA	Adeno Carcinoma	N1	9	Alive	Distant	R0
55, male	PA	Epidermoid Carcinoma	N1	8	Alive	Local	R0
59, male	V	Epidermoid Carcinoma	N0	2	Died		R1
60, male	PV	Epidermoid Carcinoma	N1	4	Alive		R0

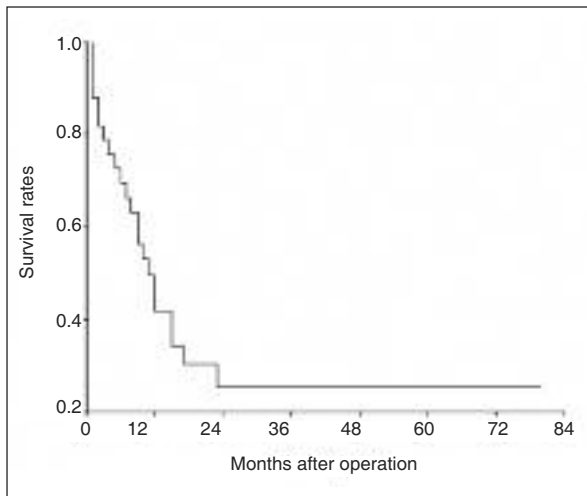
<sup>a</sup> Cases with neoadjuvant therapy,

V: Vertebra, A: Atrium, PA: Pulmonary artery, C: Carina, PV: Pulmonary vein, SVC: Superior vena cava, S: Satellite, Ao: Aorta Ep: Epidermoid, Ca: Carcinoma, C/I: Complete/Incomplete, R0: Complete resection; R1: Incomplete resection (microscopic residue).

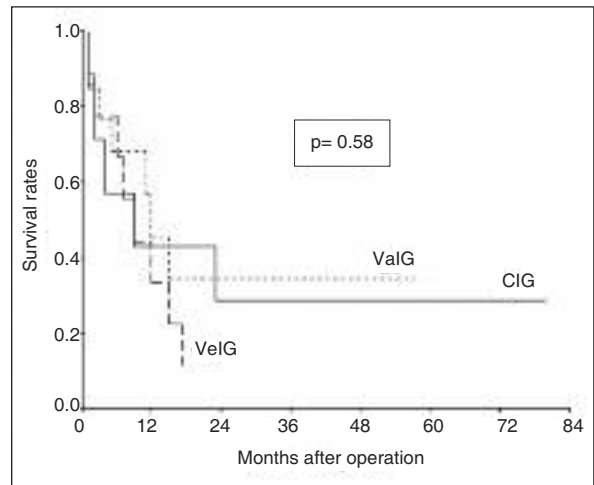
years survival rate of 42%, with a 15% operative mortality rate.<sup>10</sup> Mitchell et al concluded that nodal involvement (N2-N3) was associated with poorer prognosis and might constitute a contraindication for surgery. Among cases undergoing tracheal sleeve pneumonectomy, Darteville et al reported a five-year survival rate of 43% and an operative mortality rate of 3% in N0-1 cases, while Mitchell et al determined levels of 19% and 7%, respectively.<sup>10,11</sup> Pitz et al reported a five-year survival ra-

te of 50.9% in patients with tumors invading the trachea or carina.<sup>9</sup> With one exception, all cases with carina involvement also had trans-carinal sleeve pneumonectomy in our study. The five-year survival rate in the CIG (28.5%) was not significantly different from those in the other two groups.

The outcomes of surgical treatments for T4 tumors with left atrial and great vessel invasions are generally poor. Barlesi et al demonstrated that vas-



**FIGURE 1:** Survival curve of the 33 patients with resected T4 non-small cell lung cancer: Five years survival level was 25.3%; mean survival time was 26.7 months.



**FIGURE 2:** Survival curves of patients with resected T4 non-small cell lung cancer according to T4 subgroups: Five years survivals for the CIG (heavy line, n= 7), the VelG (thick dashed line, n= 9) and the ValG (thin dashed line, n= 13) were 28.5%, 11.1% and 34.1%, respectively. (p= 0.58) among the three groups. Median survival times for the three groups were 9, 9 and 12 months, respectively.

cular invasion despite induction treatment was a poor prognostic factor in stage 3B patients.<sup>6</sup> Watanabe et al carried out heart and great vessel resections (left atrium, superior vena cava and aorta) in a study of 31 cases and reported a five years survival rate of 16%.<sup>4</sup> In a study with the involvement of the left atrium (n= 15), superior vena cava (n= 13) and aorta (n= 5), Takahashi et al determined a five-year survival rate of 13%.<sup>8</sup> In our study, complete resection was achieved in six cases in the ValG. The five years survival rate in the ValG (34.1%) was higher than that in the other two groups, although the difference was not statistically significant. In comparison with the other studies mentioned above, this raw high ratio in our study seems noteworthy.

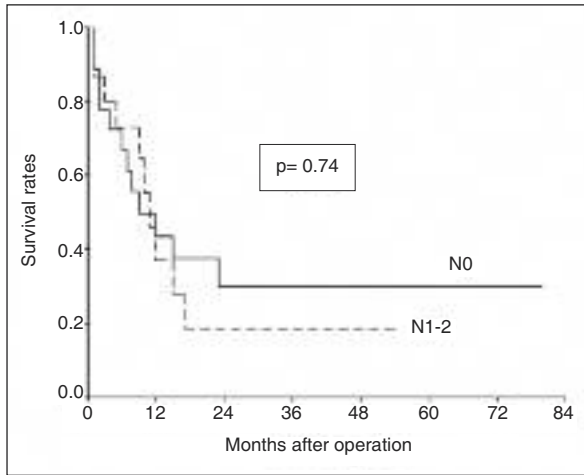
Complete resection can be achieved by resection and reconstruction of superior vena cava in patients with superior vena cava invasion.<sup>12</sup> In one multicenter retrospective study, the five years survival rate was determined as 15% after resection for superior vena cava involvement, while it was significantly higher after partial resection (p= 0.03).<sup>13</sup> Two of our cases with superior vena cava invasion were alive in postoperative month 54 and 58. No thrombosis of the superior vena cava (or superior vena cava syndrome) was observed in these patients. In the patient who underwent aortic re-

**TABLE 4:** Survival analysis with Kaplan-Meier method of T4 tumor subgroups.

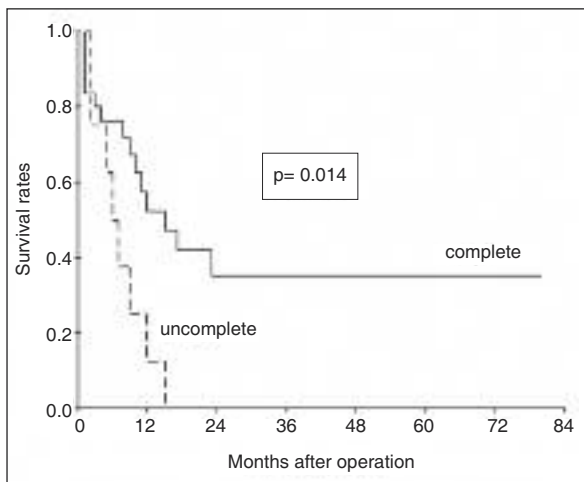
Variable	Number	Five-year survival rate (%)	P
<b>T4 subgroups</b>			
CIG	7	28.5	0.58
VelG	9	11.1	
ValG	13	34.1	
<b>Pathological N status</b>			
N0	18	30	0.74
N1-2	15	18.4	
<b>Completeness of resection</b>			
Complete	24	34.9	0.014
Incomplete	9	0	
<b>Histopathology</b>			
Epidermoid carcinoma	22	28.8	0.48
Adenocarcinoma	9	26.6	
Large cell carcinoma	2	0	
<b>Localization</b>			
Upper lobe	16	22.0	0.64
Lower lobe	5	20	
Hilum	11	29.0	
Middle lobe	1		

CIG: Carinal Invasion Group, VelG: Vertebral Invasion Group, ValG: Vascular Invasion Group.

section, embolectomy was performed for the peripheral arterial embolism that developed despite anticoagulant therapy.



**FIGURE 3:** Survival curves of patients with pathological N0 (heavy line, n= 18) and N1-2 (dashed line, n= 15) status: five-year survival level was 30% for N0 patients and 18.4% for N1-2 patients ( $p= 0.74$ ). Median survival time was 9 months for N0 patients and 11 months for N1-2 patients.



**FIGURE 4:** Survival curves of patients with complete (heavy line, n= 24) and incomplete (dashed line, n= 9) resection: the five years survival rate was 34.9% for complete resection and 0% for incomplete resection ( $p= 0.014$ ). Median survival time was 15 months for complete and 6 months for incomplete resection.

Vertebral invasion used to be considered a contraindication for surgery. However, advances in spinal surgery have afforded new opportunities. Grunewald et al argued that en bloc resection was a good option in selected cases with vertebral involvement.<sup>14</sup> They performed en bloc resection in 19 patients and achieved complete resection in 15 cases (79%); local recurrence developed in nine ca-

ses. They reported levels of 59% and 14% for one- and five years predicted survival, respectively. We failed to achieve complete resection in five of our nine cases with vertebral involvement. The longest postoperative survival time was 17 months in the VeIG and only one case was still alive in month 17 of follow-up in this group. We believe that a multidisciplinary approach during the assessment of patients with vertebral involvement and multidisciplinary collaboration in surgical intervention would yield a better outcome.

Although different approaches have been tried in cases with disseminated pleural involvement and malignant effusion, there is no perfect treatment modality accepted at present. In our clinic, we do not perform resection in such cases if the malignant nature of the effusion was proved preoperatively. We had one patient with preoperative clear effusion, which finally yielded malignant cytology. He underwent left lower lobectomy and was still alive in postoperative month 32.

Five years survival rates were 30% in N0 and 18.4% in N1-2 cases, although the difference was not statistically significant ( $p= 0.74$ ). This may be attributed to the low number of patients with N2 disease in this series. In the study by Doddoli et al, the median survival time in N2 cases was two times lower than that of N0-1 cases, even if the difference did not reach the statistical significance level.<sup>7</sup> Izbicki et al also reported that they had determined no significant difference between survival times with regard to the status of the lymph node involvement in T4 tumors.<sup>15</sup> However, the number of cases in these studies was also limited. N2 status has been especially branded as an indicator of poor prognosis in the literature.<sup>2,5,16</sup>

Three cases with N2 disease in this series were operated in the period that PET-CT was not available. Mediastinoscopy was not performed in two of them because they had no mediastinal lymph nodes preoperatively. The other patient underwent mediastinoscopy due to lymph nodes on thorax-CT scan; metastasis was reported in definitive his-

topathologic evaluation of subcarinal lymph node where frozen section was negative. There was no false negative case in our series for mediastinal lymph node evaluation after PET-CT had become available. On the other hand, it has been recommended that routine PET and mediastinoscopy are recommended for all potentially resectable patients with T4 tumors and resection only for those with N0-1 nodal status.<sup>17</sup>

Some locally advanced tumors may become operable after induction chemo-radiotherapy.<sup>2,18</sup> However, induction therapy can lead to an increase in postoperative morbidity.<sup>2,6,19</sup> We achieved complete resection in three out of four cases who received induction therapy. In two cases, we used induction therapy in order to establish better control of the disease. One patient who had positive margin as in situ carcinoma despite large tracheal sleeve resection developed BPF, and the other patient had post-pneumonecrotic empyema without BPF. No complication was observed in two patients who underwent surgery after neoadjuvant therapy for N2 disease.

## RESTRICTIONS OF THE STUDY

The number of patients in this series was small for statistical analysis by Kaplan-Meier method especially when divided into subgroups. However, it is difficult to obtain larger series in operated cases with T4 lung cancer. The largest series from a single center had 60-90 patients.

## CONCLUSIONS

T4 NSCLC has a number of subgroups. Despite the fact that the number of cases in our study was limited, our assessment based on the involvement of mediastinal organ and lymph node(s) indicated better survival rates in the CIG and VaIG groups and in patients without lymph node involvement. However, there was no statistically significant prognostic difference between the groups. The extended resections tried in these tumors carry a high risk of morbidity and mortality. The risk can be reduced by an experienced team of surgeons. Surgery should be tried, and better prognosis can be expected in selected patients, especially if complete resection is performed.

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