

## Survival Among Post-Operative Non-Small Cell Lung Cancer Patients Receiving Chemoradiotherapy; A Retrospective Analysis

Mustafa KANDAZ<sup>1</sup>, Yaren KANDAZ<sup>2</sup>, Atalay BALSARAK<sup>1</sup>, Kaan AYDOĞDU<sup>1</sup>, Emin MAMMADOV<sup>1</sup>, Fatma YILDIZ<sup>1</sup>

<sup>1</sup>Department of Radiation Oncology, Karadeniz Technical University Faculty of Medicine, Trabzon-Turkey

<sup>2</sup>Karadeniz Technical University Faculty of Medicine, Trabzon-Turkey

Orcid: <https://orcid.org/0000-0003-1106-6227><sup>1</sup>

### ABSTRACT

**Background:** Despite being the second most frequent malignancy, lung cancer is the main reason for cancer-related fatalities. In this study, patients who underwent surgery for Non-Small Cell Lung Cancer and received adjuvant chemoradiotherapy will be evaluated.

**Patients and Methods:** The data of 123 eligible patients who were operated with the diagnosis of Non-Small Cell Lung Cancer between 2000 and 2020 and who were treated with adjuvant chemoradiotherapy were retrospectively analyzed.

**Results:** Of the 123 patients that were included in the study, 111 (90%) were males and 12 (10%) were females. The mean age was 62.11±8.92 (range:33-77) years. According to histological types, 65 (53%) patients were squamous cell carcinoma, 54 (44%) patients were adenocarcinoma and 4 (3%) patients were large cell carcinoma. Fifty-nine (48%) patients had undergone right lobectomy, 43 (35%) patients left lobectomy, 7 (6%) patients right pneumonectomy and 14 (11%) patients had left pneumonectomy. Mean OS time of all patients was 63.34±5.98 (51.62-75.07) months. One, 2, 3 and 5-year survival rates were 89.9%, 66.9%, 56.3% and 40.9%, respectively. There was a significant correlation between the T stage (p=0.05) of the disease and the chemotherapy protocol (p=0.046) and survival.

**Conclusion:** Complete surgical resection remains the most effective treatment for patients with operable Non-Small Cell Lung Cancer. The high risks of distant recurrence brought on by the presence of metastatic disease that went unnoticed prior to surgery, however, restrict the effectiveness of surgical resection. Therefore, postoperative chemoradiotherapy employing constrained areas and contemporary approaches can be advantageous.

**KEYWORDS:** Non-Small Cell Lung Cancer, Surgery, Adjuvant chemoradiotherapy.

### ARTICLE DETAILS

**Published On:**  
**07 September 2023**

**Available on:**  
<https://ijmscr.org/>

### INTRODUCTION

Despite being the second most frequent malignancy, lung cancer is the main reason for cancer-related fatalities.<sup>[1]</sup> Non-Small Cell Lung Cancer (NSCLC) is the most typical histological type. Typically, 10% of patients are in stage I, 20% are in stage II, 30% are in stage III, and 40% are in stage IV at the time of diagnosis.<sup>[2]</sup> Surgery is advised for patients in stages I–IIIA. However, even after total resection, stage IA patients had a 5-year survival rate of 70–80% compared to stage IIIA patients' 20–25%. Even in individuals who receive surgery in the early stages, recurrence occurs in about 20–30% of cases.<sup>[3]</sup> Lymphadenectomy is not routinely advised in the management of NSCLC. Various centers conduct

radical systematic mediastinal lymphadenectomy, radiological worrisome lymph node excision, and mediastinal lymph node sampling.<sup>[4]</sup>

In the postoperative radiotherapy (PORT) study conducted by The Lung Cancer Study Group, the use of both preoperative and postoperative chemotherapy and radiation therapy in patients undergoing surgery to improve both local control and survival have been examined, and it was reported that especially mediastinal lymph node involvement worsened the prognosis. Additionally, it was demonstrated that while chemotherapy or concurrent therapy enhanced local control and disease-free survival, they had no impact on overall survival (OS).<sup>[5]</sup>

## Survival Among Post-Operative Non-Small Cell Lung Cancer Patients Receiving Chemoradiotherapy; A Retrospective Analysis

This study aims to evaluate patients who were operated on with the diagnosis of NSCLC. Its relationships with surgery will be examined, including OS, 1, 2, 3, and 5-year survival.

### MATERIALS AND METHODS

#### Patient selection

The study was conducted on 123 patients who were diagnosed with NSCLC cancer, treated and followed between January 2000 to December 2020 in our clinic. This retrospective analysis (Project No. 2021-34) received approval from the institutional review board. The information about patients was accessed with the retrospective analysis of patient files. Sex (male/female), age ( $\leq 59/\geq 60$ ), localization (right, left), histology (large cell carcinoma (LCC), adenocarcinoma (ADC), squamous cell carcinoma (SCC)), stage of the disease (TNM), and treatment modality were noted. The study did not include participants with metastatic disease.

#### Treatment

During treatment, patients are typically lying on their backs with their torsos supported and partially immobilized by movable wingboards. More options are available when using lateral or oblique beam angles when the arms are positioned above the head. For radiotherapy (RT) application, computer tomography (CT) scans were conducted. The mass or mass stump and lymph nodes were fused with pre-operative CT or Positron Emission Tomography (PET)-CT. The heart, esophagus, and medulla spinalis were contoured as critical organs. The 3-dimensional conformal radiotherapy (3DRT) technique was used. In RT planning, the mass/mass bed was defined as clinical tumor volume (CTV1) and lymph nodes as CTV2. The planned target volume (PTV) was created by giving a 2 cm margin to CTV1 and a 1 cm margin to CTV2. The RT indication, if N2 was 50-54 Gy, if the positive margin was 54-60 Gy, or if there was a gross residual tumor, a dose of 60-66 Gy was administered.

#### Chemotherapy

Cisplatin 75 mg/m<sup>2</sup> day 1, vinorelbine 25 mg/m<sup>2</sup> days 1 and 8, every 21 days for 4 cycles, gemcitabine 1250 mg/m<sup>2</sup> days 1 and 8, cisplatin 75 mg/m<sup>2</sup> day 1, docetaxel 75 mg/m<sup>2</sup> day 1, every 21 days for 4 cycles, or paclitaxel 45–50 mg/m<sup>2</sup> weekly were used as the chemotherapy protocol.

#### Follow-up

Patients were followed clinically every three months for the first two years, every six months for the next three years, and then once a year after that. Each appointment included a physical examination and a chest CT scan. Recurrence or metastasis was defined as a recurrence that was confirmed by a biopsy or as evidence of disease progression on successive imaging scans. Local recurrence or distant metastasis were the two main groupings of failure patterns that were described.

#### Statistical methods

Based on OS rates, clinical outcome was examined. The relationship between patient variables (age, sex, histology), tumor features (stage, lymph node involvement, surgery type, positive surgical margins, chemotherapy protocol, radiotherapy dose), and clinical outcome (distant metastasis and local recurrence) was examined. The Kaplan-Meier method was used to determine survival rates. In order to identify differences between subgroups and forecast variables with independent prognostic relevance on survival, the log-rank test was applied. At a computed p-value of 0.05, all significant tests and statistical significance were accepted.

### RESULTS

A hundred eleven (90%) of the 123 patients who participated in the study were male, and 12 (10%) were female. The mean age was  $62.11 \pm 8.92$  years (range: 33-77), Forty (33%) patients were  $\leq 59$  years and 83 (67%) patients were  $\geq 60$  years old.

According to histological types, 65 (53%) patients were SCC, 54 (44%) patients were ADC and 4 (3%) patients were LCC. Fifty nine (48%) patients had undergone right lobectomy, 43 (35%) patients left lobectomy, 7 (6%) patients right pneumonectomy and 14 (11%) patients had left pneumonectomy.

Twenty three (19%) patients were T1, 58 (47%) patients were T2, 27 (22%) patients were T3 and 15 (12%) patients were T4 tumor. There were no lymph node involvement in 26 (21%) patients. 26 (21%) patients had N1 and 71 (58%) patients had N2.

RT was applied to 38 (31%) patients for positive or close surgical margins, 66 (54%) patients for N2, 7 (5%) patients for surgical margins and N2, and 12 (10%) patients for recurrence.

According to clinical staging, 4 (3%) patients were stage IA, 10 (8%) were stage IIA, 26 (21%) were stage IIB, 57 (47%) were stage IIIA and 26 (21%) patients were stage IIIB.

Twenty-two (18%) patients were treated with 50 Gy, 36 (29%) patients with 54 Gy, 33 (27%) patients with 60 Gy and 32 (26%) patients were treated with 66 Gy.

Of the patients with good general condition and performance, 57 (47%) received cisplatin + vinorelbine, 27 (22%) cisplatin + docetaxel, and 32 (26%) cisplatin + gemcitabine. Weekly paclitaxel was administered to the other 7 (5%) patients.

Progression was detected in 27 (22%) of the patients during the follow-up. Six (5%) of them were in the surgical stump and 21 (17%) of them were in mediastinal lymph nodes.

Metastases were detected in 44 (36%) of the patients during the follow-up. Eighteen (15%) of them were in the brain, 16 (13%) of them were in bone, 7 (6%) of them were in the contralateral lung and 3 (2%) of them were in the surrenal

## Survival Among Post-Operative Non-Small Cell Lung Cancer Patients Receiving Chemoradiotherapy; A Retrospective Analysis

gland. Metastases were seen after a mean of  $24.3 \pm 20.94$  (range: 5-96) months from the date of diagnosis. Bone metastases were seen at  $38.7 \pm 26.7$  (range: 6-96) months, brain metastases at  $13.64 \pm 9.88$  (range: 3-32) months, and contralateral lung metastases at  $12.5 \pm 10.6$  (range: 5-20) months on average.

In the follow-up, two patients had bladder cancer and one patient had endometrial cancer. All of these patients had N2 and received cisplatin+dosectaxel chemotherapy. Forty-nine (40%) of the study's patients were still alive and 74 (60%) had passed away at the time of the last follow-up.

### Survival

A total of 123 patients for whom information was available were evaluated in the survival analysis. All patients' mean OS duration was  $63.34 \pm 5.98$  (51.62-75.07) months. The overall 1-, 2-, 3-, and 5-year survival rates were 89.9%, 66.9%, 56.3%, and 40.9%, respectively (Figure 1.).

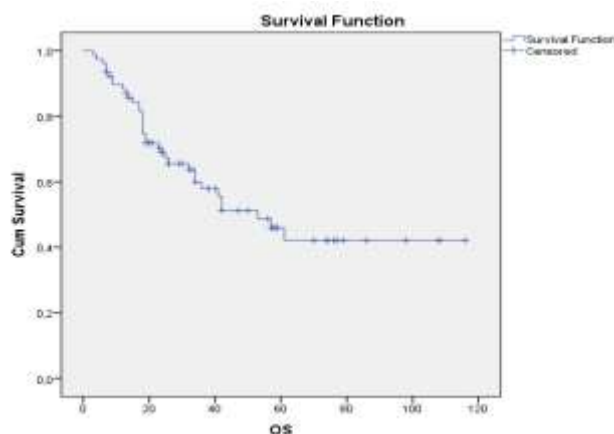


Figure 1. Overall survival

The mean OS time of the patients  $\leq 59$  years of age was  $71.79 \pm 9.77$  (52.63-90.95) months. The proportions of survivors at 1, 2, 3, and 5 years were, respectively, 96.2%, 72%, 67.5%, and 50%. The mean OS time of patients  $\geq 60$  years of age was  $55.57 \pm 7.19$  (41.46-69.68) months. The rates of survival at 1, 2, 3, and 5 years were 82.9%, 64.2%, 50%, and 33.8%, respectively. There was no statistically significant difference ( $p = 0.313$ ) in OS time between the two groups.

The mean OS for males was  $61.08 \pm 6.38$  (48.58-73.59) months. For males, 1, 2, 3 and 5-year OS rates were 87.5%, 75%, 60% and 60%, respectively. Mean OS time for females was  $57.95 \pm 9.74$  (38.84-77.50) months. Females had survival rates of 88.9%, 66%, 53.9%, and 42.4% at 1, 2, 3, and 5 years, respectively. There was no statistically significant difference in OS time between the sexes ( $p = 0.351$ ).

For patients with SCC histology, the mean OS time was  $58.22 \pm 7.96$  (42.61-73.84) months. The rates of survival at 1, 2, 3, and 5 years were 90.3%, 55.9%, 51.9%, and 40.9%, respectively. For patients with an ADC histology, the mean OS time was  $68.71 \pm 8.72$  (51.61-87.81) months. One, 2, 3 and 5-year survival rates were 88.9%, 80%, 68.5% and 51.7%,

respectively. For patients with an LCC histology, the mean OS time was  $28.7 \pm 13.5$  (2.04-54.96) months. One, 2, and 3-year survival rates were 50%, 50%, 50% and 51.7%, respectively. No patient was alive at 5 years. There was no statistically significant difference ( $p = 0.247$ ) in OS time between the three groups.

The mean OS in patients who underwent right lobectomy was  $63.7 \pm 8.16$  (47.79-79.80) months. In these patients, the 1, 2, 3 and 5-year survival rates were 87.2%, 68.2%, 54.3% and 42.3%, respectively. Mean OS in patients who underwent left lobectomy was  $61.21 \pm 9.57$  (42.53-79.89) months. In these patients, the 1, 2, 3 and 5-year survival rates were 93.6%, 72.2%, 61.8% and 48.1%, respectively. Mean OS in patients who underwent right pneumonectomy was  $56.8 \pm 11.8$  (33.65-79.94) months. In these patients, the 1, 2, 3 and 5-year survival rates were 80%, 80%, 80% and 80%, respectively. Mean OS in patients who underwent left pneumonectomy was  $41.22 \pm 16.55$  (8.78-73.66) months. In these patients, the 1, 2, 3 and 5-year survival rates were 74.1, 29.6%, 29.6% and 29.6%, respectively. Between the surgical methods in terms of OS time, no statistically significant difference ( $p = 0.282$ ) was seen.

When the patients are analyzed for T stages, in T1 patients mean OS time was  $44.71 \pm 6.73$  (31.51-57.90) months. One, 2, 3 and 5 years survival rates were 88.7%, 73.3%, 54.3% and 54.3%, respectively. In T2 patients mean OS time was  $69.24 \pm 7.7$  (54.14-84.34) months. One, 2, 3 and 5 years survival rates were 97.2%, 73.2%, 62.7% and 49.8% respectively. In T3 patients mean OS time was  $63.3 \pm 13.02$  (37.76-88.84) months. One, 2, 3 and 5 years survival rates were 82.6%, 63.6%, 54.5% and 43.6%, respectively. In T4 patients mean OS time was  $22.7 \pm 5.42$  (12.07-33.32) months. One and 2 years survival rates were 60% and 40% respectively and no patient lived 3 years. There was a significant relationship between disease T stage and survival. Survival of T1, T2 and T3 patients was significantly better than that of T4 patients ( $p = 0.05$ ) (Figure 2.).

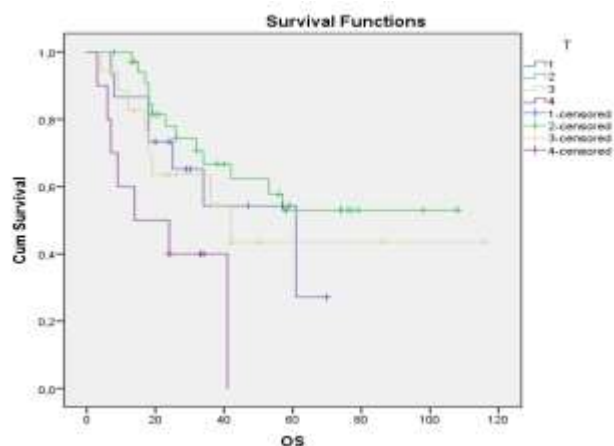


Figure 2. Survival by T stage

When the patients are analyzed for N stages, in N0 patients mean OS time was  $43.5 \pm 6.48$  (30.80-56.20) months. One, 2,

## Survival Among Post-Operative Non-Small Cell Lung Cancer Patients Receiving Chemoradiotherapy; A Retrospective Analysis

3 and 5 years survival rates were 82.4%, 64.2%, 57% and 39.9%, respectively. In N1 patients mean OS time was 80.39±12.90 (55.09-105.68) months. One, 2, 3 and 5 years survival rates were 93.8%, 80.4%, 62% and 62%, respectively. In N2 patients mean OS time was 58.74±7.41 (44.21-73.28) months. One, 2, 3 and 5 years survival rates were 86.6%, 64.7%, 55.1% and 40.8%, respectively. There was no significant difference between the three groups (p = 0.111).

When the patients are analyzed by stages, stage IA3 mean OS time was 61.08±6.38 (48.58-73.59) months. One, 2, 3 and 5-year survival rates were 100%, 100%, 100% and 100%, respectively. Stage IIA mean OS time was 48.17±9.67

(29.21-67.14) months. One, 2, 3 and 5-year survival rates were 85.7%, 71.4%, 53.6% and 35.7%, respectively. Stage IIB mean OS time was 61.85±11.85 (38.62-85.09) months. One, 2, 3 and 5-year survival rates were 94.1%, 69.7%, 53.8% and 44.8%, respectively. Stage IIIA mean OS time was 71.10±8.94 (53.57-88.64) months. One, 2, 3 and 5-year survival rates were 91.6%, 69.5%, 61.6% and 50.2%, respectively. Stage IIIB mean OS time was 34.71±8.87 (17.30-52.11) months. One, 2, 3 and 5-year survival rates were 76.5%, 51.3%, 38.5% and 19.3%, respectively. There was no significant relation between disease stage and OS (p = 0.334). Patient characteristics and survival are shown in table 1.

**Table 1. Patient characteristics and survival.**

	n(%)	OS Mean(95%CI)	OS 1 yr (%)	OS 2 yr(%)	OS 3yr(%)	OS 5 yr(%)	p
<b>GENERAL</b>		63.34±5.98 (51.62-75.07)	89.9	66.9	56.3	40.9	
<b>AGE</b> (62.11±8.92 (33-77)							
≤ 59	40 (33%)	71.79±9.77 (52.63-90.95)	96.2	72	67.5	50	0.313
≥ 60	83 (67%)	55.57±7.19 (41.46-69.68)	82.9	64.2	50	33.8	
<b>SEX</b>							
Female	12 (10%)	61.08±6.38 (48.58-73.59)	87.5	75	60	60	0.351
Male	111 (90%)	57.95±9.74 (38.84-77.50)	88.9	66	53.9	42.4	
<b>HISTOLOGY</b>							
Squamous cell carcinoma	65 (53%)	58.22±7.96 (42.61-73.84)	90.3	55.9	51.9	40.9	0.247
Adenocarcinoma	54 (44%)	68.71±8.72 (51.61-87.81)	88.9	80	68.5	51.7	
Large cell carcinoma	4 (3%)	28.7±13.5 (2.04-54.96)	50	50	50	-	
<b>SURGERY TYPE</b>							
Right Lobectomy	59 (48)	63.7±8.16 (47.79-79.80)	87.2	68.2	54.3	42.3	0.282
Left Lobectomy	43 (35%)	61.21±9.57 (42.53-79.89)	93.6	72.2	61.8	48.1	
Right Pneumonectomy	7 (6%)	56.8±11.8 (33.65-79.94)	80	80	80	80	
Left Pneumonectomy	14 (11%)	41.22±16.55 (8.78-73.66)	74.1	29.6	29.6	29.6	
<b>T</b>							
1	23 (19%)	44.71±6.73 (31.51-57.90)	86.7	73.3	54.3	54.3	0.05
2	58 (47%)	69.24±7.7 (54.14-84.34)	97.2	73.2	62.7	49.8	
3	27 (22%)	63.3±13.02 (37.76-88.84)	82.6	63.6	54.5	43.6	
4	15 (12%)	22.7±5.42 (12.07-33.32)	60	40	-	-	
<b>N</b>							
0	26 (21%)	43.5±6.48 (30.80-56.20)	82.4	64.2	57	39.9	0.111
1	26 (21%)	80.39±12.90 (55.09-105.68)	93.8	80.4	62	62	
2	71 (58%)	58.74±7.41 (44.21-73.28)	86.6	64.7	55.1	40.8	
<b>STAGE</b>							
IA	4 (3%)	61.08±6.38 (48.58-73.59)	100	100	100	100	
IIA	10 (8%)	48.17±9.67 (29.21-67.14)	85.7	71.4	53.6	35.7	

## Survival Among Post-Operative Non-Small Cell Lung Cancer Patients Receiving Chemoradiotherapy; A Retrospective Analysis

IIB	26 (21%)	61.85±11.85 (38.62-85.09)	94.1	69.7	53.8	44.8	0.334
IIIA	57 (47%)	71.10±8.94 (53.57-88.64)	91.6	69.5	61.6	50.2	
IIIB	26 (21%)	34.71±8.87 (17.30-52.11)	76.5	51.3	38.5	19.3	

When the patients are evaluated according to radiotherapy indication, in patients with positive or close surgical margins mean OS time was 58.86±10.27 (38.72-79) months. One, 2, 3 and 5 years survival rates were 83.5%, 61.2%, 44.9% and 39.3%, respectively. In N2 positive patients mean OS time was 63.76±7.58 (48.89-78.63) months. One, 2, 3 and 5 years survival rates were 88.4%, 70.9%, 61% and 49.9%, respectively. In patients with both positive and close surgical margins and N2 positive mean OS time was 51.75±3.32 (10.98-24.01) months. One and 2 years survival rates were 75% and 75%, respectively and no patient lived 3 years. In patients who underwent radiotherapy for recurrence mean OS time was 68.4±14.28 (40.4-96.39) months. One, 2, 3 and 5 years survival rates were 87.5%, 75%, 75% and 40%, respectively. There was no significant difference between the groups (p=0.453).

When we analyzed radiotherapy doses, the patients who received 50 Gray radiotherapies had a mean OS time of 50.70±9.50 (32.08-69.32) months. One, 2, 3 and 5 years survival rates were 92.9%, 65%, 54.2% and 54.2%, respectively. In patients who received 54 Gray radiotherapies, the mean OS time of 86.34±8.56 (69.56-103.12) months. One, 2, 3 and 5 years survival rates were 87%, 82.6%, 76.3% and 76.3%, respectively. In patients who received 60 Gray radiotherapies, mean OS time was 51.62±9.99 (32.02-71.21) months. One, 2, 3 and 5 years survival rates were 77.3%, 53.1%, 47.8% and 29.8%, respectively. In patients who received 66 Gray, the mean OS time was 50.64±9.15 (32.70-68.57) months. One, 2, 3 and 5 years survival rates were 80.5%, 65.5%, 45.9% and 26.2%, respectively. There was no significant difference between the groups according to the dose of radiotherapy (p=0.084).

When we analyzed chemotherapy protocols, the patients who received cisplatin+vinorelbine chemotherapy had a mean survival time of 63.55±8.31(47.25-79.85) months. One, 2, 3 and 5 years survival rates were 83.7%, 68.6%, 61.1% and 51.7%, respectively. In patients who received cisplatin+docetaxel chemotherapy, the mean OS time of 48.27±10.87 (26.95-69.59) months. One, 2, 3 and 5 years survival rates were 83.3%, 50%, 43.7% and 29.2%, respectively. In patients who received cisplatin+gemcitabine chemotherapy, the mean OS time of 81.25±11.22 (59.26-103.24) months. One, 2, 3 and 5 years survival rates were 100%, 83%, 60.3% and 60.3%, respectively. In patients who received weekly paclitaxel chemotherapy, the mean OS time of 29.25±11.14 (7.40-51.09) months. One, 2 and 3 years survival rates were 75%, 50% and 25% respectively and no patient lived 5 years. Survival of patients receiving cisplatin+vinorelbine chemotherapy and cisplatin+gemcitabine chemotherapy was significantly better (p = 0.046). Treatment characteristics and survival are shown in table 2.

**Table 2. Treatment characteristics and survival**

	n(%)	OS Mean (95% CI)	OS rate 1 yr (%)	OS rate 2 yr (%)	OS rate 3 yr (%)	OS rate 5 yr (%)	p
<b>RT INDICATION</b>							
Surgical Marjin	38 (31%)	58.86±10.27 (38.72-79)	83.5	61.2	44.9	39.3	0.453
N2	66 (54%)	63.76±7.58 (48.89-78.63)	88.4	70.9	61	49.9	
Surgical Marjin +N2	7 (5%)	17.5±3.32 (10.98-24.01)	75	75	-	-	
Recurrence	12 (10%)	68.4±14.28 (40.4-96.39)	87.5	75	75	40	
<b>RT DOSE</b>							
50 Gy	22 (18%)	50.70±9.50 (32.08-69.32)	92.9	65	54.2	54.2	0.084
54 Gy	36 (29%)	86.34±8.56 (69.56-103.12)	87	82.6	76.3	76.3	
60 Gy	33 (27%)	51.62±9.99 (32.02-71.21)	77.3	53.1	47.8	29.8	
66 Gy	32 (26%)	50.64±9.15 (32.70-68.57)	80.5	65.5	45.9	26.2	
<b>CHEMOTHERAPY</b>							
Cisplatin+Vinorelbine	57 (47%)	63.55±8.31 (47.25-79.85)	83.7	68.6	61.1	51.7	

## Survival Among Post-Operative Non-Small Cell Lung Cancer Patients Receiving Chemoradiotherapy; A Retrospective Analysis

Cisplatin+Docetaxel	27 (22%)	48.27±10.87 (26.95-69.59)	83.3	50	43.7	29.2	0.046
Cisplatin+Gemcitabine	32 (26%)	81.25±11.22 (59.26-103.24)	100	83	60.3	60.3	
Paclitaxel	7 (5%)	29.25±11.14 (7.40-51.09)	75	50	25	-	

At the final follow-up, 49 (40%) patients were alive and 74 (60%) patients were dead.

### DISCUSSION

The most prevalent non-cutaneous cancer and the leading cause of cancer-related death worldwide is lung cancer.<sup>[1]</sup> NSCLC accounts for 80–85% of lung cancer cases. NSCLC has three primary subtypes: SCC, ADC (including bronchioalveolar), and LCC. Because their prognoses and treatments are frequently similar, several subtypes of NSCLC, which originate from many types of lung cells, are classified together.

Older people are more likely to develop lung cancer as the majority of lung cancer patients are in their seventh or later decade and the incidence before the age of 45 is very low. When diagnosed, most persons are around 70 years old.<sup>[6]</sup> Our patients ranged in age from 33 to 77, with a mean age of 62.11 + 8.92 years. One patient was in the fourth decade, six were in the fifth, twenty were in the sixth, fifty-five were in the seventh, and forty-one were in the eighth.

Although NSCLC is not related to gender, it is more common in males. However, young females are starting to experience it more frequently. One of the main reasons for this increase is that the females have started smoking. The female/male ratio in the studies was found to be 1-2/4.<sup>[7,8]</sup> The female to male ratio in our study was determined to be 1 in 9. The male gender has been demonstrated to be a poor predictor of outcome in several studies. In one study, the 5-year OS rates for men were 57.3% and for women were 76.2%.<sup>[8]</sup> In a different study, the projected survival for males at one and five years was 51% and 15%, respectively, whereas it was 60% and 19% for females. In particular for patients with stage III/IV illness or adenocarcinoma, men had a significantly higher mortality risk than women after receiving a diagnosis of NSCLC (adjusted relative risk: 1.20, 95% CI: 1.11, 1.30).<sup>[9]</sup> In our study, although females had a trend of higher survival rates, it was not statistically significant.

More than 40% of lung cancers, 60% of NSCLC, and more than 70% of surgically resected cases are adenocarcinoma, the most prevalent kind of lung cancer. About 20% of lung malignancies are SCCs. Recently, their occurrence has started to fall, probably as a result of a shift in smoking habits. LCCs account for less than 3% of lung cancers.<sup>[10]</sup> In our study, 53% of patients had SCC, 44% had ADC, and 3% had LCC. Over a 10-year study period, squamous cell carcinoma came out on top in our analysis. Squamous cell carcinoma remains the most prevalent histological type when all of those individuals are combined, even if its values are quite similar to those of adenocarcinoma and the difference is not significant. In comparison to other

distributions, this one is unique. Although the rate of change varies across different geographical locations, there is a global trend toward a rise in the proportion of adenocarcinomas and a decrease in squamous cell carcinomas.<sup>[11]</sup> Histology has not been specified in the literature as a prognostic or predictive variable in NSCLC investigations. The data contradict certain research that suggested patients with adenocarcinoma or nonsquamous histologies would have better outcomes, and other studies that suggested patients with squamous cell carcinoma would have better outcomes.<sup>[12,13]</sup> Studies are showing better survival in ADC<sup>[14]</sup> or better survival in SCC.<sup>[15]</sup> Although SCC and ADC patients had better survival than LCC patients in our study, statistical significance was not found.

Many studies have shown that surgical lobectomy both reduces postoperative complication and mortality rates and increases survival.<sup>[7,16]</sup> Suen et al. showed that the lobectomy's operational mortality and long-term survival rate were comparable to pneumonectomy's.<sup>[17]</sup> In our series, when patients who underwent lobectomy and pneumectomy were compared, no difference in survival was found.

In order to identify patient groups with comparable survival and treatment options, the stage grouping of the TNM subsets was created. Since pathological staging can be done accurately in surgical patients, survival rates are better. The 5-year survival rate for NSCLC patients drastically declines with stage. Many studies have found a difference in survival between stages.<sup>[7,18]</sup> In one study, the mean survival rate was 61% for patients with stage IA disease, 38% for stage IB disease, 34% for stage IIA disease, 13% for stage IIIA disease, 5% for stage IIIB disease, and 1% for stage IV disease.<sup>[19]</sup> In our series, although there was no statistical difference between the stages, there was a survival difference according to the T stage, and there was no patient who lived for 3 years among the T4 patients. Numerous studies demonstrate that in non-small cell lung cancer, the number of positive lymph nodes is a potent independent predictive predictor.<sup>[20]</sup> However, in our study, although N1 patients had a better survival, no statistical difference was found.

Many different chemotherapy regimens can be used concurrently with RT. However, several studies have shown that cisplatin-based chemotherapy regimens improve survival. A retrospective analysis of the prospective ANITA research, in which patients received concomitant chemoradiotherapy, showed the effectiveness of PORT and cisplatin-vinorelbine.<sup>[21]</sup> In our study, patients who underwent adjuvant treatment with cisplatin+vinorelbine and

## Survival Among Post-Operative Non-Small Cell Lung Cancer Patients Receiving Chemoradiotherapy; A Retrospective Analysis

cisplatin+gemcitabine had a superior 5-year survival rate ( $p = 0.046$ ).

Postoperative radiation decreased patient survival in stage I and stage II patients in 1998, but not in stage III disease, according to the PORT meta-analysis. The results of the PORT meta-analysis have been questioned in a number of ways. For instance, the majority of the included studies used cobalt-60 devices, an outdated radiotherapy technology, which linear accelerators are now the norm, and several studies used dosages that are now viewed as suboptimal per fraction.<sup>[22]</sup> Results from non randomized subanalyses of two trials have more recently added to the discussion. First, radiation for N2 disease was related with higher survival rates, according to the big SEER database.<sup>[23]</sup> Second, stage IIIA patients receiving radiation in both the observation and treatment arms of the ANITA study had greater 5-year OS rates than N2 patients who did not receive postoperative radiation.<sup>[24]</sup> Collectively, these findings suggest that the lower mortality risk associated with radiotherapy itself may outweigh the benefit of postoperative radiation in terms of treating microscopic mediastinal lymph node disease. Postoperative radiation has been used in the past as an adjuvant therapy to improve local control. Studies have employed total doses of 30 to 60 Gy divided into 2-2.5 Gy fractions. Currently, it is unknown what the ideal dose of postoperative thoracic radiation should be. In our series, we applied 60-66 Gy radiotherapy to patients with a gross residual tumor, 50-54 Gy to patients with N2 disease and 54-60 Gy to patients with positive borders.

According to a Mountain revision, patients with NSCLC had a stage IA disease rate of 61%, a stage IB disease rate of 38%, a stage IIA disease rate of 34%, a stage IIIA disease rate of 13%, a stage IIIB disease rate of 5%, and a stage IV disease rate of 1%.<sup>[25]</sup> Fang et al. came to the conclusion that the 5-year survival rate was 72.0% in stage IA and 61.0% in stage IB, 32.9% in stage IIA, 34.5% in stage IIB, 22% in stage IIIA, 6 and 15.9% in stage IIIB, and 7.1% in stage IV after conducting a retrospective review of 1,905 operated NSCLC cases. In our study, the 5-year survival rate for stage IA3 patients was 100%, stage IIA patients' was 35.7%, and stage III patients' was 44.8%.<sup>[7]</sup>

### STUDY LIMITATIONS

Only resected instances were included in this retrospective registry. The study cohort is relatively small, it spans a considerable amount of time, and it only involves one institution and one facility. Additionally, a wide range of variables, such as the surgeon, hospital volume, surgeon experience, radiation oncologist's experience, and postoperative care, can affect the patient's survival.

### CONCLUSION

The most successful course of action for patients with operable NSCLC continues to be complete surgical resection.

The high risks of distant recurrence brought on by the presence of metastatic disease that went unnoticed prior to surgery, however, restrict the effectiveness of surgical resection. As a result, adjuvant treatments have been researched to see if they can increase survival and lower rates of local and distant recurrence. Adjuvant RT lowers local relapse rates following resection while chemotherapy has a systemic effect. After lung cancer resection, individuals who receive RT may experience improved local control and survival. Additionally, systemic and local therapies probably work conjointly, so advancements in systemic staging and therapy may enhance the efficacy of local therapies to boost OS. Therefore, employing confined areas and cutting-edge techniques, postoperative radiotherapy and chemotherapy can be advantageous. For NSCLC patients who have an indication for adjuvant therapy after primary tumor resection surgery, more research is necessary to determine the optimal course of action.

### REFERENCES

- I. Torre LA, Siegel RL, Jemal A. Lung Cancer Statistics. *Adv Exp Med Biol* 2016;893:1-19.
- II. Kawachi R, Tsukada H, Nakazato Y, Takei H, Furuyashiki G, Koshi-ishi Y, et al. Early recurrence after surgical resection in patients with pathological stage I non-small cell lung cancer. *Thorac Cardiovasc Surg*. 2009;57(8):472-5.
- III. Wahl M, Gubens MA, and Yom SS. Handbook of evidence-based radiation oncology. 3rd edition. Non-small Cell Lung Cancer, Eds Hansen EK, March Roach M. Springer International Publishing AG, pp 2018;293-322.
- IV. Izbicki JR, Passlick B, Pantel K, Pichlmeier U, Hosch SB, Karg O, et al. Effectiveness of radical systematic mediastinal lymphadenectomy in patients with resectable non-small cell lung cancer: results of a prospective randomized trial. *Ann Surg* 1998;227:138-144.
- V. The Lung Cancer Study Group. The benefit of adjuvant treatment for resected locally advanced non-small-cell lung cancer. *J Clin Oncol* 1988;6:9-17.
- VI. Howlander N, Noone AM, Krapcho M, Garshell J, Miller D, Altekruse SF, et al. SEER Cancer Statistics Review, 1975-2011, National Cancer Institute. <http://seer.cancer.gov/archive/csr/1975-2011>, 2014.
- VII. D Fang, D Zhang, G Huang, R Zhang, L Wang, D Zhang. Results of Surgical Resection of Patients With Primary Lung Cancer: A Retrospective Analysis of 1,905 Cases. *Ann Thorac Surg* 2001;72:1155-1159.
- VIII. Yoshida Y, Murayama T, Sato Y, Suzuki Y, Saito H, Nomura Y. Gender Differences in Long-Term

## Survival Among Post-Operative Non-Small Cell Lung Cancer Patients Receiving Chemoradiotherapy; A Retrospective Analysis

- Survival after Surgery for Non-Small Cell Lung Cancer. *Thorac Cardiovasc Surg* 2016;64(6):507-14.
- IX. Visbal AL, Williams BA, Nichols FC 3rd, Marks RS, Jett JR, Aubry MC, et al. Gender differences in non-small-cell lung cancer survival: an analysis of 4,618 patients diagnosed between 1997 and 2002. *Ann Thorac Surg* 2004;78(1):209-215.
- X. Lewis DR, Check DP, Caporaso NE, Travis WD, Devesa SS. US lung cancer trends by histologic type. *Cancer* 2014;120(18):2883-2892.
- XI. Escuin JS, Sorribes ML, Arca JA, Ares AN, Hernández JH, Jover AMC, et al. The EpiclicP-2003 study: A multicenter epidemiological and clinical study of lung cancer in Spain. *Arch Bronconeumol* 2006;42:446-452.
- XII. Fossella F, DeVore R, Kerr R, Crawford J, Natale RR, Dunphy F, et al. Randomized phase III trial of docetaxel versus vinorelbine or ifosfamide in patients with advanced non-small cell lung cancer previously treated with platinum-containing chemotherapy regimens. *J Clin Oncol* 2000;18:2354-2362.
- XIII. Saynak M, Aksu G, Fayda M, Kaytan E, Oral E, Gurocak S, et al. The results of concomitant and sequential chemoradiotherapy with cisplatin and etoposide in patients with locally advanced non-small cell lung cancer. *J BUON* 2005;10:213-218.
- XIV. Asamura H, Goya T, Koshiishi Y, Sohara Y, Eguchi K, Mori M, et al. A Japanese Lung Cancer Registry study: prognosis of 13,010 resected lung cancers. *J Thorac Oncol* 2008;3(1):46-52.
- XV. Loncarevic O, Acimovic S, Vukovic J, Stojisavljevic M, Maric N, Loncarevic S, et al. Overall survival of patients with non-small cell lung cancer after surgery treatment. *Vojnosanit Pregl* 2018;75(12):1157-1164.
- XVI. Yoshino I, Yokoyama H, Yano T, Ueda T, Takai E, Mizutani K, et al. Comparison of the surgical results of lobectomy with bronchoplasty and pneumonectomy for lung cancer. *J Surg Oncol* 1997;64:32-35.
- XVII. Suen HC, Meyers BF, Guthrie T, Pohl MS, Sundaresan S, Roper CL, et al. Favorable results after sleeve lobectomy or bronchoplasty for bronchial malignancies. *Ann Thorac Surg* 67;1999:1557-1562.
- XVIII. Koike T, Terashima M, Takizawa T, Aoki T, Watanabe T, Akamatsu H. Results of surgery for primary lung cancer based on the new international staging system. *Jpn J Thorac Cardiovasc Surg* 1999;47:313-317.
- XIX. Zarogoulidis K, Zarogoulidis P, Kaid Darwiche K, Boutsikou E, Machairiotis N, Tsakiridis K, et al. Treatment of non-small cell lung cancer (NSCLC). *J Thorac Dis* 2013;5(4):389-396.
- XX. Fukui T, Mori S, Yokoi K, T. Mitsudomi T. Significance of the number of positive lymph nodes in resected non-small cell lung cancer. *J Thorac Oncol* 2006;2:120-125.
- XXI. Douillard JY, Rosell R, De Lena M, Riggi M, Hurlteloup P, Mahe MA, et al. Impact of postoperative radiation therapy on survival in patients with complete resection and stage I, II, or IIIA non-small-cell lung cancer treated with adjuvant chemotherapy: the adjuvant Navelbine International Trialist Association (ANITA) randomized trial. *Int J Radiat Oncol Biol Phys* 2008;72(3):695-701.
- XXII. Munro AJ. What now for postoperative radiotherapy for lung cancer? *Lancet* 1998;25:352(9124):250-251.
- XXIII. Lally BE, Zelerman D, Colasanto JM, Haffty BG, Dettterbeck FC, Wilson LD. Postoperative radiotherapy for stage II or III nonsmall-cell lung cancer using the Surveillance, Epidemiology, and End Results Database. *J Clin Oncol* 2006;24:2998-3006.
- XXIV. Douillard JY, Rosell R, De Lena M, Carpagnano F, Ramlau R, González-Larriba JL, et al. Adjuvant vinorelbine plus cisplatin versus observation in patients with completely resected stage IB-IIIa non-small-cell lung cancer (Adjuvant Navelbine International Trialist Association [ANITA]): A randomised controlled trial. *Lancet Oncol* 2006;7:719-727.
- XXV. Mountain CF. Revisions in the International System for Staging Lung Cancer. *Chest* 1997;111:1710-1717.