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Original Article

Results of surgery after neoadjuvant treatment for non-small cell lung cancer

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ABSTRACT

Background: In locally advanced non-small cell lung cancer, survival rates achieved only by surgical treatment are unfortunately lower than expected. It's believed that survival rates can be raised by multimodal therapies including surgery. The purpose of the study is to analyse the results of surgical treatment in patients who underwent surgical resection after neoadjuvant treatment due to locally advanced non-small cell lung cancer.

Materials and Methods: The patients who underwent lobectomy or pneumonectomy after neoadjuvant chemotherapy and/or radiotherapy due to locally advanced non-small cell lung cancer were included in this study. The patients were divided into two groups according to oncological treatment indication. Group A included patients who received neoadjuvant therapy due to T disease and group B due to N2 disease. The surgical interventions, pathological results, postoperative complications, mortality, recurrence, 5-year disease-free survival, and overall survival were analysed.

Results: 154 patients were included in the study. 142 were men and 12 were women with a mean age of 57.7 ± 16.97 (between 35 and 77). Ninety-six patients received induction therapy due to T disease, and 58 patients due to N2 disease. Pneumonectomy was performed on 41 patients, lobectomy was performed on 113 patients (18 bronchial sleeve resection). Histopathologic results revealed squamous cell carcinoma in 96 (62.3%), adenocarcinoma in 52 (33.8) and large cell carcinoma in 6 (3.9%) patients. A complete response to neoadjuvant treatment was achieved in 19 (Group A, n = 15, group B, n = 4) patients. Postoperative pathologic results showed mediastinal lymph node metastasis in 13 (13.6%) patients in group A and, in 28 (48.3%) patients in group B, which is statistically significant. Prolonged air leak was the most common complication in both groups. Operative mortality was observed in 4 (2.6%) patients. In 82 patients 47 in group A and 35 in group B recurrence or metastasis were detected during the follow-up. 5-year disease-free survival rate was 43.2% in group A and 38.4% in group B. Five- year survival rate was 46.1% in group A and 38% in group B.

Conclusions: The patients who achieved a histopathologic complete response following induction therapy had statistically significantly better disease-free and overall survival rates. Pathologically proven lymph node metastasis increased the rate of recurrence or metastasis significantly (p = 0.01). The disease-free and overall survival rate decreased significantly (p = 0.0001, p = 0.0001). It is deducible in light of these findings that patients who received neoadjuvant treatment for N2 achieved better disease-free survival and overall survival.

Keywords: lung cancer, induction therapy, lung resection

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Introduction

Non-small cell lung cancer (NSCLC) accounts for 80-85% of all lung cancers, and the treatment method that provides the best local control and survival is surgical resection [1]. Only about 20% of non-small cell lung carcinomas can be treated surgically when diagnosed, and approximately one-third are diagnosed at a locally advanced stage (stage III) [2]. Stage III covers a heterogeneous patient group. For this reason, its treatment is the most controversial group and there is still no standardized approach to definitive treatment. Locally advanced stage patients are tried to be made candidates for surgical treatment by reducing the tumor volume with neoadjuvant chemotherapy and/or radiotherapy (induction therapy) or by clearing the lymph nodes of the disease [3].

The aim of this study was to evaluate the results by analyzing the pathological diagnosis, surgical resection method, operative mortality, postoperative complications, recurrence or metastasis status, disease- free survival, and overall survival in NSCLC cases that underwent surgical resection after induction therapy.

Materials and Methods

Patients who underwent surgical intervention after induction therapy for T or N2 in locally advanced NSCLC patients between January 2010 and December 2015 were included in the study. Patients' gender, age, neoadjuvant treatment method, surgical methods, histopathological results, postoperative complications, mortality, recurrence or metastasis status, disease-free, and overall survival effects were determined. The results were revised by the new TNM staging system (according to 8th). Dr. Suat Seren Chest Disease and Thoracic Surgery Training and Research Hospital Ethics Committee approval was received for this study. (2017/3770).

The patients were divided into two groups according to oncological treatment indication. Group A included patients who received neoadjuvant therapy due to T disease such as pleural invasion, vascular invasion, superior sulcus tumors, and group B due to N2 disease.

All patients were evaluated with PET/CT before and 4 weeks after neoadjuvant treatment. EBUS and cervical mediastinoscopy were performed for invasive mediastinal staging, and Thorax CT and PET/CT were used in patients where this could not be performed. A 75% decrease in metabolic activity on PET/CT was considered as a response.

Results

During this period, a total of 905 patients underwent surgery for NSCLC, and 154 patients who were decided on induction treatment at the thorax council due to locally advanced stage and subsequently underwent lung resection were included in the study. Among these, 96 patients received induction therapy due to T disease, and 58 patients due to N2 disease. 142 (92.2%) of the patients were male, 12 (7.8%) were female, and the average age was 57.7 ± 16.97 (range 35-77). As a histopathological diagnostic method, bronchoscopy was performed in 77 (50%) of the patients and TTNAB was performed in 77 (50%). Squamous cell carcinoma was detected in 96 (62.3%) patients, adenocarcinoma in 52 (33.8%) patients, and large cell carcinoma in 6 (3.9%) patients.

Before induction treatment, mediastinal staging was performed with EBUS in 5 (5.2%) patients in Group A. Histopathological N2 was not detected. In this group, EBUS was performed in 4 (4.2%) patients and mediastinoscopy was performed in 3 (3.1%) patients for mediastinal staging after induction treatment. Before induction therapy, EBUS was performed in 17 (29.3%) patients, mediastinoscopy in 4 (6.9%) patients, and EBUS and mediastinoscopy in one (1.7%) patient for invasive mediastinal staging in Group B. While 20 of them were reported as malignant, 2 of them received induction treatment because their PET/CT findings were predicted to be false negative. When we examined the invasive mediastinal staging after induction therapy in this group of patients, no invasive procedure was performed in 33 (56.9%) patients, EBUS in 9 (15.5%), mediastinoscopy in 7 (12.1%), and EBUS and mediastinoscopy in 9 (15.5%) patients.

Of those who received induction treatment due to T, 75 (78.1%) received chemotherapy, seven (7.3%) received radiotherapy, and 14 (14.6%) received chemoradiotherapy. When we look at the dose of chemotherapy applied, 47 (49.0%) patients were administered less than 4 cycles of chemotherapy, while 42 (43.8%) patients were administered 4 or more cycles of chemotherapy. While radiotherapy was applied to 21 (21.9%) of the patients who received induction treatment due to T, when we examined the radiotherapy dose of the patients, we found that four (4.2%) patients received radiotherapy of 50 Gray or less, and 17 (17.7%) patients received radiotherapy above 50 Gray. The diagnosis of malignancy in this group was obtained by bronchoscopy in 51 (53.2%) patients before induction therapy, and by TTIAB in 45 (46.9%) patients.

Of those who received induction treatment due to N2, 55 (94.8%) received chemotherapy and 3 (5.2%) received chemoradiotherapy. When we look at the dose of chemotherapy applied, 32 (55.2%) patients were administered less than 4 cycles of chemotherapy, while 26 (44.8%) patients were administered 4 or more cycles of chemotherapy. When we examined the radiotherapy dose in patients who received induction therapy due to N2, one (1.7%) patient received radiotherapy at 50 Gray

or less, while two (3.4%) patients received radiotherapy above 50 Gray. The diagnosis was obtained by bronchoscopy in 26 (44.8%) of the patients in this group, while the TTIAB method was used in 32 (55.2%).

Lobectomy was performed in 113 (73.4%) of the patients. The most common operation was right upper lobectomy in 43 patients and left upper lobectomy in 33 patients. Bilobectomy inferior was performed in 12 patients, left lower lobectomy in 11, right lower lobectomy in eight, bilobectomy superior in five and middle lobectomy in one patient. Bronchial sleeve resection was performed in 18 (11.7%) of the patients, and pneumonectomy was performed in 41 (26.6%) (27 left, 14 right).

The most common additional procedure performed along with lung resection was pericardial resection in 57 patients. Chest wall resection was performed in 10 patients, and pericardial and chest wall resection was performed together in 3 patients. In one patient, partial resection of the superior vena cava was performed along with pericardial resection, and in another patient, partial resection of the diaphragm with pericardial resection and primary repair of the diaphragm was performed (Table 1).

Table 1. Demographic and clinical data of those who received induction therapy due to T and N2.

	Group A n(%)	Group B n(%)
Gender		
Female	7(7.3)	5(8.6)
Male	89(92.7)	53(91.4)
Histopathologic diagnosis method		
Bronchoscopy	51(53.1)	26(44.8)
TTFNAB	45(46.9)	32(55.2)
Histopathologic results		
Squamous cell carcinoma	65(66.3)	31(53.4)
Adenocarcinoma	28(28.6)	24(41.4)
Large cell carcinoma	3(5.1)	3(5.2)
Invasive mediastinal staging method		
Before induction	5(5.2)	22(37.9)
EBUS	5(5.2)	17(29.3)
Mediastinoscopy	-	4(6.9)
EBUS + mediastinoscopy	-	1(1.7)
Induction treatment		
Chemotherapy	89(92.8)	58(100)
4 cycles or less chemotherapy	47(49)	32(55.2)
More than 4 cycles of chemotherapy	42(43.8)	26(44.8)
Radiotherapy	21(21.9)	3(5.2)
Radiotherapy at 50 Gray and below	4(4.2)	1(1.7)
Radiotherapy more than 50 Gray	17(17.7)	2(3.4)
Chemoradiotherapy	14(14.7)	3(5.2)
Invasive mediastinal staging method		
After induction	14(14.6)	25(43.1)
EBUS	7(7.3)	9(15.5)
Mediastinoscopy	4(4.2)	7(12.1)
EBUS + mediastinoscopy	3(3.1)	9(15.5)
Resections		
Lobectomy	69(71.9)	44(75.9)
Pneumonectomy	27(28.1)	14(24.1)
Additional surgical procedures		
Bronchial sleeve	14(14.6)	4(6.9)
Pericardium resection	41(42.7)	16(27.6)
Chest wall resection	7(7.3)	3(5.2)
Pericardium and chest wall resection	2(2.1)	1(1.7)
Pericardium and SVC partial resection	1(1)	
Pericardium and diaphragm partial resection	1(1)	

Postoperatively in Group A, there were 15 patients reported as histopathological Tx. No lymph node metastasis was detected in 68 patients and N1 positivity was detected in 15 patients. While 5 of the patients had only N2 positivity, 8 patients had both N1 and N2 positivity. In Group B, there were 4 patients reported as histopathological Tx, and no lymph node metastasis was detected in 22 patients. 8 patients had N1positivity, 13 had only N2 positivity, and 15 patients had both N1 and N2 positivity. When the postoperative N status was examined, the most detected N status in both groups was N0, but the presence of postoperative N2 was higher in the group receiving induction therapy due to N2 and this difference was statistically significant (p = 0.0001).

According to these evaluations, 19 (12.3%) of all our cases had a complete response and were classified as Tx. Additionally, there was a regression in the tumor in 41 (26.6%) cases and they were classified as T1. 62 (40.3%) of the cases were included in the T2 group, which was the largest group. Additionally, 21 (13.6%) cases were evaluated as T3 and 11 (7.1%) as T4.

When the histopathological lymph node status was examined after surgery, 90 (58.4%) were evaluated as N0, 23 (14.9%) as N1, and 41 (26.7%) as N2. While 18 (11.6%) of the patients in the N2 group had only N2, 23 (14:9%) had both N1 and N2 lymph node metastases (Table 2).

Adjuvant treatment was given to 89 (57.8%) of the patients. The most frequently applied adjuvant treatment was chemotherapy in 63 (40.9%) patients. Additionally, 3 (1.9%) patients received radiotherapy and 23 (14.9%) patients received chemoradiotherapy.

During the follow-up, no complications were observed in 87 (56.5%) patients, while complications were observed in 67 (43.5%) patients (Table 3).

Table 2. Postoperative histopathologic results.

	Group A n(%)	Group B n(%)
T results		
Tx (Complete response)	15(15.6)	4(6.9)
T1	23(23.9)	18(31.1)
T2	34(35.4)	28(48.2)
T3	15(25.6)	6(10.3)
T4	9(9.5)	2(3.5)
N results		
N0	68(70.8)	22(37.9)
N1	15(15.6)	8(13.8)
N2	5(5.2)	13(22.4)
N1+N2	8(8.4)	15(25.9)

Table 3. Postoperative complications.

Prolonged air leakage	42(27.3)
Expansion defect	14(9.1)
Atelectasis	15(9.7)
Pneumonia	10(6.5)
Pulmonary embolism	1(0.6)
Early period bronchopleural fistula	3(1.8)
Rethoracotomy due to hemorrhage	7(4.5)
Early period bronchopleural fistula + empyema	3(1.8)
Chylothorax	3(1.8)
Wound infection	1(0.6)

When the postoperative complications that developed during the follow-up of the patients were examined, it was observed that gender and age group were not statistically significant. When pneumonectomy compared to lobectomy, the presence of a bronchoplastic procedure caused a statistically significant higher rate of postoperative complications. The type, dose, and indication of induction treatment were not a statistically significant factor in postoperative complications. Postoperative complications were detected in 43 (44.8%) patients who received induction therapy due to T and in 24 (41.4%) patients who received induction therapy due to N2, and there was no statistically significant difference between the two groups (p = 0.73). Additionally, it was determined that the histopathological type of the tumor and postoperative T and N status were not statistically significant factors in postoperative complications.

Operative mortality occurred in four (2.6%) patients, two patients in each age group, and there was no statistically significant difference. Operative mortality was statistically significantly higher in female gender (p = 0.03). In addition, it was determined that the presence of lobectomy, pneumonectomy, bronchoplasty, and the type and dose of induction therapy did not statistically affect operative mortality. Operative mortality was detected in two (2.1%) patients who received induction therapy due to T and in two (3.4%) patients who received induction therapy due to N2 which was not statistically significant (p = 0.62).

Although recurrence or metastasis was detected in 47 (49%) patients who received induction therapy due to T and 35 (60.3%) patients who received induction therapy due to N2, there was no statistically significant difference between the two groups (p = 0.18). However, the patients who received induction radiotherapy doses above 50 Gray had a lower rate of recurrence or metastasis than others, and this was statistically significant

(p = 0.04). In addition, a higher rate of recurrence or metastasis was detected in patients whose tumor histopathological type was reported as adenocarcinoma compared to others, and this was statistically significant (p = 0.01). When we examined the effect of the postoperative T group, it was found that as the T of the tumor increased, a higher rate of recurrence or metastasis was detected, as expected, and this was statistically significant (p = 0.01). Additionally, postoperative lymph node metastasis is similar; It was observed that as the lymph node metastasis positivity group increased, more relapses or metastases were detected and this was statistically significant (p = 0.01).

The best 5-year survival rate, 94.7%, was found in the Tx group, where no viable tumor was detected postoperatively and was evaluated as a complete response to induction therapy. In the others, 5-year survival rates were found to be 40.4% in the T1 group, 31.6% in T2, 21.4% in T3 and 51.9% in T4. Postoperative T status was found to have a statistically significant effect on survival (p = 0.004). Figure 1 shows the analysis of the effect of postoperative T status on survival.

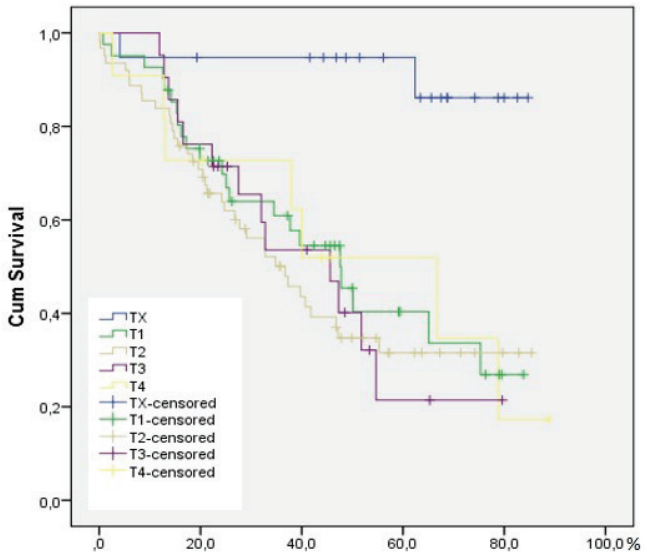

Figure 1. Analysis of the effect of postoperative T status on survival.

When we look at the effect of lymph node metastasis on survival, there was a 5-year survival rate of 51.2% in the N0 group. Hilar lymph node metastasis (N1) was detected in 48.4%, and mediastinal lymph node metastasis (N2) in 51.1%. In the N1+N2 group, 5-year survival was not determined. The effect of postoperative N status on 5-year survival was found to be statistically significant (p = 0.0001).

The effect of the postoperative T and N status of the patients on disease-free survival, as expected, was; that as the T factor and the lymph node metastasis group increased, the disease-free survival was worse and this was statistically significant (p = 0.008, p = 0.0001 respectively).

During the average 37.7 ± 23.3 (0.1-88.7) month follow-up of all patients, no recurrence or metastasis was detected in 72 (50%) patients. While 17 (11%) of them lived with recurrence or metastasis, 65 (42.2%) had mortality after recurrence or metastasis. When the factors affecting the development of recurrence or metastasis were examined, it was observed that no statistically significant difference was found in terms of age group, gender, operation type, presence of bronchoplasty, induction therapy indication group, type and chemotherapy dose.

When the study was completed, 73 (47.4%) of the patients were alive (56 patients without disease, 17 patients with recurrence or metastasis) and 81 (52.6%) patients were dead (65 patients due to recurrence or metastasis and 16 patients due to reasons other than disease). After an average follow-up of 37.7 ± 23.3 (0.1-88.7) months, the 5-year survival rate of the patients was 43.1%. Median survival was found to be 47.3 months and average survival time was 51.1 months.

The 5-year survival rate was 46.1% in those treated for T and 38% in those treated for N2, and there was no statistically significant difference between the two groups (p = 0.28). Although the 5-year survival rate was higher in women compared to men, in those who underwent pneumonectomy compared to lobectomy, and in those who did not undergo bronchoplastic procedure compared to those who did not, no statistically significant difference was detected. Figure 2 shows the disease-free survival analysis with the neoadjuvant treatment group.

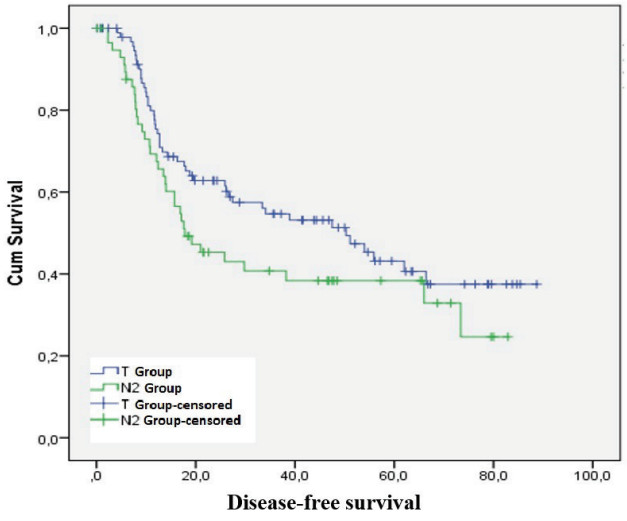

Figure 2. Disease-free survival analysis with neoadjuvant treatment group.

When the effect of the histopathological type of the tumor on disease-free survival was considered, large cell carcinoma had a 5-year disease-free survival rate of 83.3%. 5-year disease-free survival was found to be 45% in squamous cell carcinoma and 28.1% in adenocarcinoma, and the difference between the two was statistically significant ($p = 0.04$).

The type of induction therapy, its dose, and additional surgical procedures in groups no significance on survival was detected. When the effect of adjuvant treatment on recurrence or metastasis was considered, a lower rate of relapse or metastasis was present in those who did not receive adjuvant treatment, while the highest rate of relapse or metastasis was detected in the group receiving chemoradiotherapy as adjuvant treatment, and this was statistically significant ($p = 0.007$).

The 5-year survival rate was 51.5% in patients who did not receive adjuvant treatment and 16.9% who received adjuvant chemoradiotherapy, and the difference was statistically significant ($p = 0.004$).

Statistical Analysis

SPSS 24 Package Program was used in this retrospective study. Comparative analyses of the groups were made using "Fisher's Exact Test" and "Pearson Chi-Square test". The “Kaplan-Meier” method was used in survival analyses. Statistical analyses were performed using the "log-rank" method for survival comparisons between groups. $P < 0.05$ was considered significant.

Discussion

Long-term survival in non-small cell lung cancer is determined by multiple factors [2]. The most important determinants are tumor stage, determined by tumor size (T), lymph node metastasis (N), and distant metastasis (M) [4]. While surgical resection is recommended as the first treatment option for best survival in early-stage NSCLC, multimodal treatment options are used in locally advanced NSCLC [2]. Induction treatments are preferred in locally advanced NSCLC because they reduce tumor size, increase the likelihood of complete resection, and prevent micrometastases [5,6]. Although studies have not definitively shown that neoadjuvant treatment increases survival, neoadjuvant treatment is preferred by many clinicians because non-surgical oncological treatment does not provide the desired success in locally advanced NSCLC patients, postoperative adjuvant treatment is poorly tolerated by the patient, and most patients cannot complete the treatment [7,8].

Pneumonectomy accounts for 10-25% of lung resections performed for non-small cell lung cancer [9,10]. It has been reported that the rate of pneumonectomy increases in post-neoadjuvant surgeries [10]. In addition to pneumonectomy being a disease in itself, the importance of sleeve resections has increased due to the higher mortality rate and the higher probability of postoperative major complications. Stamatis et al commented that, while the lobectomy rate was 66%, bronchial sleeve lobectomy was performed in 14% in their series [10]. Lobectomy was performed in 113 (73.4%) patients in our study, and 18 of them underwent bronchial sleeve lobectomy. These rates show a similar correlation to large series. The presence of a bronchoplastic procedure did not have a statistically significant effect on recurrence or metastasis, disease-free survival and overall survival. However, it was determined that postoperative complications were observed in 13 (72.2%) of 18 patients who underwent bronchoplastic procedures and this was statistically significant ($p = 0.01$). Similarly, while no statistically significant effect was detected on recurrence or metastasis, disease-free survival and overall survival in patients who underwent lobectomy, postoperative complications were detected in 57 (50.4%) of those who underwent lobectomy and in 10 (24.4%) of those who underwent pneumonectomy and were statistically significant ($p = 0.005$). The rate was lower in our study after pneumonectomy. However, while more major complications such as bronchopleural fistula were observed after pneumonectomy, more minor complications such as expansion defect and prolonged air leakage were observed in the presence of lobectomy or bronchoplasty.

Neoadjuvant treatment can be applied as chemotherapy, radiotherapy, or chemoradiation, depending on the indication. Kirn et al primarily recommend chemotherapy as induction therapy in N2 patients with locally advanced NSCLC. In their study, they found that induction chemotherapy increased survival compared to radiotherapy in N2 patients [11]. Westeel et al in their French intergroup study, examined the induction chemotherapy dose and the timing of chemotherapy in 528 patients. In this study, patients who received 2 cycles of chemotherapy and 4 cycles of chemotherapy preoperatively were examined. Additionally, patients who received all 4 cycles of chemotherapy before surgery, 2 cycles before surgery, and 2 cycles after surgery were compared. At the end of this study, it was

observed that the chemotherapy dose did not make a difference in terms of effectiveness, timing, survival and morbidity [12]. In the study by Sonett et al, among 40 patients, it was found that preoperative radiotherapy applied to patients over 45 Gray increased postoperative complications, but there was no difference in terms of operative mortality, recurrence or metastasis, and survival [13]. In our study, no statistically significant effect of the type of induction treatment was detected on operative mortality, postoperative complications, recurrence or metastasis, disease-free survival and overall survival.

In the review written by Candela et al for mediastinal evaluation after induction therapy, it was determined that thorax CT, PET-CT and remediastinoscopy had a false negative rate of up to 20%. Better results have been obtained with needle biopsy methods such as EBUS and EUS. It has been determined that mediastinoscopy is the most reliable method for mediastinal staging and the false negative rate increases in the case of remediastinoscopy. For this reason, it has been suggested that the initial evaluation should be made with needle methods such as EBUS or EUS, and that mediastinoscopy would be more appropriate for re-evaluation after induction treatment [14]. In our study, the methods used in mediastinal invasive staging were in line with the literature. While EBUS was used more before induction treatment, the rate of mediastinoscopy increased after induction treatment. As expected, post-treatment invasive mediastinal staging was used at a statistically significantly higher rate in those who received induction therapy due to N2 ($p = 0.001$).

In a study, 57% of the patients who underwent lung resection after induction therapy were found to have squamous cell carcinoma, 32% to adenocarcinoma, and 11% to large cell carcinoma. Similarly, in our study, squamous cell carcinoma was detected at a higher rate. In their study, it was stated that the histopathological type of the tumor did not have a statistically significant effect on survival, but the presence of squamous cell carcinoma was a better prognostic factor [15]. In our study, it was found that a higher rate of recurrence or metastasis developed in adenocarcinomas and this was statistically significant ($p = 0.01$). However, no statistically significant effect of the histopathological type of the tumor on operative mortality and survival was detected. When we examined the effect of histopathological type on disease-free survival, the 5-year disease-free survival rates were found to be 45% in squamous cell carcinoma, 28.1% in adenocarcinoma and 83.3% in large cell carcinoma. The highest 5-year disease survival rate was found in large cell carcinoma and the lowest in adenocarcinoma, and the difference was statistically significant ($p = 0.04$).

Junker et al and Cyjon et al's studies evaluated the effect of pathological T status on survival in patients who underwent lung resection after induction therapy. Junker et al grouped the patients with the best response rate to induction therapy as grade I and, those with the lowest response rate as grade III and compared the 3-year survival of the patients. As a result of the Junker study, a 3-year survival rate of 56% in grade I and 11% in grade III was obtained, and it was determined that the response rate to treatment had a statistically significant effect on survival [16,17]. Cyjon et al divided tumors into groups according to tumor size and made a second tumor size classification, using 4 centimeters (cm) as a limit, as under 4 cm and over 4 cm. In their study, survival decreased as tumor size increased, and the median survival time for tumors less than 4 cm was calculated as 17 months, and for tumors larger than 4 cm, the median survival time was calculated as 14 months, and a statistically significant difference was found between the two groups [17]. When literature data are examined, the complete response rate to induction therapy varies between 5-15%. It has been determined that a complete response to treatment is a very important factor in terms of survival. In the study conducted by Mouillet et al, 5-year survival was found to be 80.1% in patients with a pathological complete response, while it was 44.8% in those without a complete response, and a statistically significant difference was detected ($p < 0.0001$) [18]. In our study, when we examined the effect of postoperative T status on disease-free survival, the highest 5-year disease-free survival was in the Tx group with 74.4%. Although the 5-year disease-free survival rate was lower as the group of postoperative T status increased, the 5-year disease-free survival of the T3 group was lower than the T4 group. Postoperative T status was found to have a statistically significant effect on disease-free survival ($p = 0.008$). When we examined the effect of postoperative T status on overall survival, the highest 5-year overall survival rate was in the Tx group with 94.7%. It was determined that postoperative T status had a statistically significant effect on the overall survival of the patients ($p = 0.004$). It was determined that induction therapy had a statistically significant effect on both disease-free survival and overall survival, especially in cases of complete response. Although both overall survival

and disease-free survival rates decreased as the postoperative T factor increased, it was observed that the rate in the T4 group was higher than the T3 group in both parameters.

In the study by Yoshino et al, although the 5-year overall survival rate was 35% in patients with only N2 positivity, this rate was stated to be 13% in N1+N2 positivity [19]. As expected, it was observed that as the lymph node metastasis group increased, the survival rate decreased and the worst group was the N1+N2 group. In the literature, the 5-year survival rate of patients who underwent lung resection after induction chemotherapy in case of mediastinal lymph node positivity detected by mediastinoscopy is given as 30-40% [20]. In our study, although 5-year overall survival was not observed in patients with hilar and mediastinal lymph node positivity, others had a 5-year overall survival rate of up to 50%. In the study conducted by Sause et al, the 3-year survival rate of patients in whom lymph node metastasis was not detected in the mediastinal lymph nodes by radiological evaluation and mediastinoscopy, but in whom mediastinal lymph node metastasis was detected in the pathological examination of resection samples, was found to be approximately 50% [21].

Decker et al argued that adjuvant chemotherapy is more effective than radiotherapy in reducing the risk of distant metastasis. However, in patients with positive surgical margins and a high risk of local recurrence, simultaneous chemoradiation was recommended before adjuvant chemotherapy [22]. In our study, a 41.5% rate of recurrence or metastasis was detected in those who did not receive adjuvant treatment and this rate was found to be 82.6% in those receiving chemoradiotherapy. It was thought that this was because patients with a higher postoperative stage needed adjuvant treatment, and as the stage increased, the need for multimodality treatment in adjuvant treatment increased.

In conclusion, it was determined that, patients who responded well to neoadjuvant treatment and whose stage regressed after treatment had better survival outcomes after surgery. We believe that after neoadjuvant treatment with an experienced team, all surgical interventions, including pneumonectomy and bronchoplastic procedures, can be performed with acceptable mortality, morbidity and complication rates.

Declaration of conflicting interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

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Ethics approval

This study was approved by Health Sciences University, Dr. Suat Seren Chest Disease and Thoracic Surgery Training and Research Hospital Ethics Committee (2017/3770).

Authors' contribution

TY; Concept, design, literature search, data acquisition, writing the article AU; data analysis, statistical analysis, manuscript preparation, manuscript editing and manuscript review, SY,ÖS,SG; supervision, manuscript review.

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