Original Article / Özgün Makale

Extended resections in the treatment of locally advanced lung cancer

Lokal ileri evre akciğer kanseri tedavisinde genişletilmiş rezeksiyonlar

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ÖΖ

ABSTRACT

Background: This study aims to evaluate surgical outcomes and prognosis in patients who underwent extended lung resection for locally advanced lung cancer.

Methods: Between January 2015 and December 2019, a total of 61 patients (60 males, 1 female; mean age: 61.7±12.2 years; range, 32 to 90 years) with locally advanced non-small-cell lung cancer who underwent extended lung resection were retrospectively analyzed. Data including age, sex, comorbid diseases, symptoms, smoking status, pulmonary function test results, tumor location, methods used for preoperative tissue diagnosis, histopathological cell type, type of surgical resection, pathological stage, nodal involvement, postoperative complications, types of adjuvant therapy, and mortality rate were recorded. Survival and the factors affecting survival were examined.

Results: Seven (11.4%) patients had Stage IIIB, 40 (65.5%) patients had Stage IIIA, and 14 (22.9%) patients had Stage IB disease. Intrapericardial pneumonectomy accounted for 30 (49.1%) of all extended lung resections. Chemotherapy was administered to 31 (50.8%) patients and chemoradiotherapy to 24 (39.3%) patients in the postoperative period. In the survival analysis, 70-month survival rate was calculated as 63.9% and the median survival was 48 months. There was a statistically significant association between survival with adjuvant chemotherapy and chemoradiotherapy (p=0.003). The mortality rate at 70 months of follow-up was 36.1%.

Conclusion: Extended lung resection contributes significantly to the improvement of survival rates in carefully selected locally advanced cases. Particularly with adjuvant chemotherapy, local recurrences can be prevented, and survival rates can be improved.

Keywords: Chemotherapy, extended resection, locally advanced disease, lung cancer.

Amaç: Bu çalışmada lokal ileri akciğer kanseri nedeniyle genişletilmiş akciğer rezeksiyonu yapılan hastaların cerrahi sonuçları ve prognozu değerlendirildi.

Çalışma planı: Ocak 2015 - Aralık 2019 tarihleri arasında küçük hücreli dışı akciğer kanseri nedeniyle genişletilmiş akciğer rezeksiyonu yapılan toplam 61 hasta (60 erkek, 1 kadın; ort. yaş: 61.7±12.2 yıl; dağılım, 32-90 yıl) retrospektif olarak incelendi. Yaş, cinsiyet, eşlik eden hastalıklar, semptomlar, sigara içme durumu, solunum fonksiyon testi sonuçları, tümörün yeri, ameliyat öncesi doku tanısı için kullanılan yöntemler, histopatolojik hücre tipi, cerrahi rezeksiyon tipi, patolojik evre, nodal tutulum, ameliyat sonrası komplikasyonlar, adjuvan tedavi çeşitleri ve mortalite oranı kaydedildi. Sağkalım ve sağkalıma etki eden faktörler incelendi.

Bulgular: Yedi (%11.4) hastada Evre IIIB, 40 (%65.5) hastada Evre IIIA ve 14 (%22.9) hastada Evre IB hastalık izlendi. İntraperikardiyal pnömonektomi tüm genişletilmiş akciğer rezeksiyonlarının 30'unu (%49.1) kapsıyordu. Ameliyat sonrası dönemde 31 (%50.8) hastaya kemoterapi ve 24 (%39.3) hastaya kemoradyoterapi verildi. Sağkalım analizinde 70 aylık sağkalım oranı %63.9 olarak hesaplandı ve medyan sağkalım 48 ay idi. Adjuvan kemoterapi ve kemoradyoterapi (p=0.003) arasında istatistiksel olarak anlamlı bir ilişki saptandı (p=0.003). Yetmiş aylık takipte mortalite oranı %36.1 idi.

Sonuç: Dikkatlice seçilmiş lokal ileri evre olgularda genişletilmiş akciğer rezeksiyonu, sağkalım oranlarının iyileşmesine ciddi katkılar sağlamaktadır. Özellikle adjuvan kemoterapi ile birlikte, lokal nükslerin önüne geçilebilmekte ve sağkalım oranları iyileştirilebilmektedir.

Anahtar sözcükler: Kemoterapi, genişletilmiş rezeksiyon, lokal ileri hastalık, akciğer kanseri.

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It was presented as an oral presentation at the UASK 2022 Congress March 18, 2022, Antalya, Türkiye. Received: February 21, 2023 Accepted: April 23, 2023 Published online: October 19, 2023 Cite this article as: Topaloğlu Ö, Türkyılmaz A, Karapolat S, Buran A, Tekinbaş C. Extended resections in the treatment of locally advanced lung cancer. Turk Gogus Kalp Dama 2023;31(4):538-546. doi: 10.5606/tgkdc.dergisi.2023.24788.

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This is an open access article under the terms of the Creative Commons Attribution-NonCommercial License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes (http://creativecommons.org/licenses/by-nc/4.0(). Only 15 to 25% of lung cancer cases are operable at the time of diagnosis, and 25 to 35% of these are in Stage I-II. On admission, up to 30% of patients present with locally advanced disease.^[1] Extended lung resection is the term used to describe the surgical removal of the lung together with the tissues and organs that the tumor has infiltrated in cases of locally advanced lung cancer.^[2]

Surgery is the only course of action for the treatment of lung cancer that has been scientifically proven and offers a chance of recovery. Therefore, utilization of surgical treatment techniques is unavoidable. Surgical procedures are the most effective treatment method in patients with local, resectable and advanced, but R0 resectable lung cancer.

In the present study, we aimed to evaluate surgical outcomes in patients who underwent extended lung resection for lung cancer.

PATIENTS AND METHODS

This single-center, retrospective study was conducted at Karadeniz Technical University, Faculty of Medicine, Department of Thoracic Surgery between January 2015 and December 2019. A total of 61 patients (60 males, 1 female; mean age: 61.7±12.2 years; range, 32 to 90 years) with locally advanced (Stage IIIA and IIIB) non-small-cell lung cancer (NSCLC) who underwent extended lung resection were included. Data including age, sex, comorbidities, radiological findings, preoperative diagnosis, surgery, pathology results and survival of the patients were obtained from the hospital information management system and patient files.

All patients underwent preoperative medical history taking and physical examination, routine laboratory tests, pulmonary function tests, arterial blood gas examinations, posteroanterior and lateral chest radiographs, thoracic computed tomography (CT) and distant organ scans (cranial magnetic resonance imaging [MRI], abdominal CT, whole body bone scintigraphy). Abdominal CT and bone scintigraphy were not performed in patients undergoing positron emission tomography (PET)/CT. Patients with limited respiratory function were evaluated using perfusion scintigraphy and diffusing capacity of the lungs for carbon monoxide (DLCO). Lymph node sampling by mediastinoscopy or thoracoscopic biopsy was performed in those who were suspected to have N2 disease on radiological examination.

Data regarding survival and treatment stages in expanded lung resections were obtained.

Statistical analysis

Statistical analysis was performed using the SPSS version 15 software (SPSS Inc., Chicago, IL, USA). Descriptive data were expressed in mean \pm standard deviation (SD), median (min-max) or number and frequency, where applicable. Frequency, percentage, standard deviation for mean and interquartile range for median values were used for demographic and perioperative data. Survival of the patients was calculated according to the date of death or last control. Survival rates were calculated using the Kaplan-Meier survival analysis. A *p* value of <0.05 was considered statistically significant.

RESULTS

The most common comorbidity was hypertension in 20 (32%) patients. Respiratory function test and DLCO test were applied to 50 (82%) patients. Preoperative imaging was performed with PET/CT method in 54 (88.5%) patients, and pathological diagnosis was made in 58 (95%) patients with transthoracic fine needle aspiration biopsy (TTNAB) and endobronchial ultrasound (EBUS) method. Neoadjuvant therapy was given to six (9.8%) of the patients. Neoadjuvant chemotherapy was applied to five (8.2%) patients due to the detection of single N2 positivity in the preoperative invasive mediastinal examination, and neoadjuvant chemoradiotherapy (CRT) was applied to one (1.6%) patient for a T4 tumor. Demographic data, comorbidities, respiratory function test results, preoperative pathological diagnostic methods, and the reasons for neoadjuvant treatment of all patients are shown in detail in Table 1.

The most common extended resection operation was intrapericardial pneumonectomy in 30 (49.1%) patients. The second most frequently performed extended resection operation was thoracic wall resection (*en bloc*). Extended surgical methods applied to the patients are presented in Table 2.

Squamous cell carcinoma was the most common neoplasm in 36 (59%) patients in cell typing after pathological examinations. Lymph node involvement according to the pathological examination results revealed N0 lymph node positivity in 28 (45.9%), N1 lymph node positivity in 23 (37.7%), and N2 lymph node positivity in 10 (16.4%) patients. After pathological examination, 14 (22.9%) patients were in Stage IIB, 40 (65.5%) patients were in Stage IIIA, and seven (11.4%) patients were in Stage IIIB. Following the pathological examinations, the cell typing, lymph node involvement, resection completeness, tumors

Characteristics	n	%	Mean±SD	Min-Max
Age (year)			61.7±12.2	32-90
Sex				
Male	60			
Female	1			
Comorbidity				
Hypertension	20	32.8		
Diabetes mellitus	6	9.8		
COPD	6	9.8		
Coronary artery disease	5	8.2		
Myocardial infarction	1	1.6		
Benign prostatic hyperplasia	1	1.6		
Larynx carcinoma	1	1.6		
Renal cell carcinoma	1	1.6		
Colon carcinoma	1	1.6		
Pulmonary function test (PFT)*				
FEV ₁			72.6±20.197	
FEV ₁ <50%	7	11.5		
$\text{FEV}_1 \ge 50\%$	43	70.5		
DLCO <20	16	26.2		
DLCO ≥20	34	55.7		
Type of preoperative diagnosis				
TTNAB	29	47.5		
EBUS	29	47.5		
Neoadjuvant treatment recipients	6	9.8		
Receiving CT for the presence of N2	5	8.2		
Receiving CRT for T4 tumor	1	1.6		

Table 1. Demographic and cli	nical data of patients (n=61)
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SD: Standard deviation; COPD: Chronic obstructive pulmonary disease; FEV1: Forced expiratory volume in 1 second; DLCO: Diffusing capacity of the lungs for carbon monoxide; TTNAB: Transthoracic needle aspiration biopsy; EBUS: Endobronchial ultrasound; CT: Chemotherapy; CRT: Chemoradiotherapy; * PFT could not be performed due to the limited respiratory functions of 11 cases in the study.

Table 2. Extended resection types of patients

Extended resection type	n	%
Intrapericardial pneumonectomy		
Right pneumonectomy	14	22.9
Left pneumonectomy	15	24.6
Left pneumonectomy and esophageal resection	1	1.6
Thoracic wall resection (en bloc)		
Right upper lobectomy	7	11.4
Right inferior bilobectomy	3	5
Right lower lobectomy	4	6.5
Left upper lobectomy	2	3.2
Left lower lobectomy	4	6.5
Left lower lobectomy + diaphragmatic resection	1	1.6
Tracheal sleeve pneumonectomy (carinal pneumonectomy)		
Right pneumonectomy + carinal resection	8	13.1
Vertebra resection		
Right upper lobectomy	1	1.6
Vena cava superior resection		
Right upper lobectomy	1	1.6

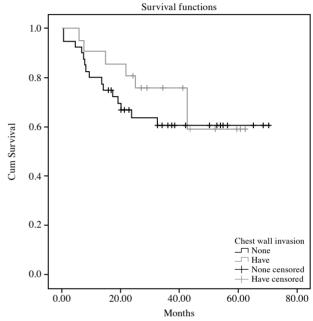
smaller than T4 and T4 tumors and staging of the tumors are shown in detail in Table 3.

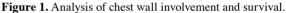
The most common postoperative complication was pneumonia in 14 (23%) patients. Respiratory complications were observed in four (6.6%) patients with a forced expiratory volume in 1 sec (FEV1) value below 50% and in six (9.8%) patients with a DLCO value below 20 mL/min/mmHg (Table 3).

Characteristics	n	%
Pathologic examination result		
Squamous cell carcinoma	36	59
Adenocarcinoma	12	20
Large cell carcinoma	5	8
Adenoid cystic carcinoma	4	6
Sarcoma	2	3
Combined carcinoma	1	2
Giant cell carcinoma	1	2
N status as a result of pathologic examination		
NO	28	45.9
N1	23	37.7
N2	10	16.4
Resection completeness		
R0	57	93.4
R1	4	6.6
Dethologic exemination result t status	-	
Pathologic examination result t status Tumors <t4< td=""><td>35</td><td>57.4</td></t4<>	35	57.4
T4 tumors	26	42.6
	20	42.0
Pathologic examination result stage		22 0
Stage IIB	14	22.9
T3N0M0	14	22.9
Stage IIIA	40	65.5
T2N2M0	3	4.9
T3N1M0	15 14	24.6
T4N0M0 T4N1M0	14 8	22.9 13.1
Stage IIIB	8 7	15.1 11.4
T3N2M0	3	4.9
T4N2M0	3 4	4.9 6.5
	4	0.5
Postoperative complications		• •
Pneumonia	14	23
Atelectasis	9	14.8
Pleural effusion	8	13.1
Bronchopleural fistula	4	6.6
Atrial fibrillation	4	6.6
Hemothorax Wound gits infection	1	1.6
Wound site infection	1	1.6
Receiving adjuvant treatment		
Receiving chemotherapy	31	50.8
Receiving chemoradiotherapy	24	39.3
Out of treatment	6	9.8

In the postoperative period, 31 (50.8%) patients received chemotherapy and 24 (39.3%) patients received CRT. Although adjuvant treatment was recommended to six (9.8%) patients, no treatment was given according to their demand (Table 3).

After follow-up, 22 (36.1%) patients died, and 39 (63.9%) patients survived. While there was no procedure-related mortality, three (4.9%) patients experienced early postoperative mortality from pulmonary embolism and respiratory failure.





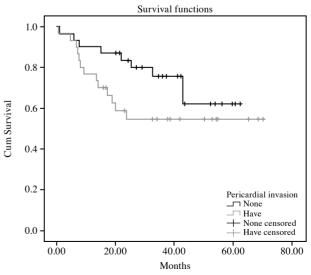


Figure 2. Analysis of pericardial involvement and survival.

The Kaplan-Meier method for survival analysis revealed an overall survival of 63.9%, one-year survival of 83.6%, and median survival of 48 months.

Univariate analysis including several factors was performed and survival analysis was carried out using Kaplan-Meier and log-rank (Mantel-Cox) method. There was no significant correlation between the type of resection and survival (p=0.283), chest wall involvement and survival (p=0.503) (Figure 1), pericardial involvement and survival (p=0.158) (Figure 2), T and survival (p=0.335)

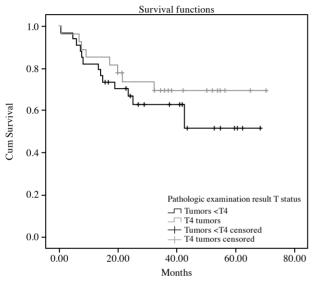


Figure 3. Analysis of pathologic examination result T status and survival.

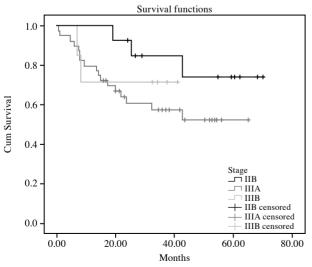


Figure 4. Analysis of disease stage and survival.

(Figure 3), and disease stage and survival (p=0.099) (Figure 4). There was a significant relationship between adjuvant therapy and survival (p=0.003) (Figure 5).

DISCUSSION

Among lung cancers, locally advanced lung cancer is a heterogeneous group that includes larger tumors with or without invasion into surrounding structures, making it less amenable to standard surgical procedures. According to the current 8th Tumor, Node, Metastasis (TNM) classification, due to the heterogeneous distribution of T4 tumors, the published series are often small and retrospective in nature.^[3] Over time, as more therapeutic options, including neoadjuvant treatments, have become available, the role of surgery for these tumors has expanded, as well.

The T3N0 subgroup in Stage IIB accounts for a small proportion of these cases. In the study conducted by Downey et al.,^[4] the five-year survival rate after complete *en bloc* resection applied due to chest wall invasion was 49%. In our study, the five-year survival rate for T3N0 patients with chest wall invasion (n=14, 23%) was 74.5% and the median survival was 60 months. Since these patients formed a homogeneous group without nodal involvement, their survival rates were found to be higher.

The heterogeneity of Stage IIIA creates differences in survival. In the literature, the survival rate for

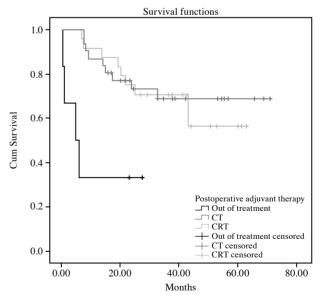


Figure 5. Analysis of adjuvant therapy and survival. CT: Computed tomography; CRT: Chemoradiotherapy.

the T3N1 subgroup varies between 25 and 30% in complete resections, while this rate decreases to 0% in incomplete resections.^[4-6] In our study, the three-year survival rate for T3N1 patients (n=15, 24.6%) was 53% and the median survival was 35 months.

Although seven (11.4%) patients in our study had Stage IIA disease as evidenced by radiological examination, postoperative pathological examination revealed T3N2 disease in three patients and T4N2 disease in the remaining patients. As there was no pathological involvement on preoperative CT and PET/CT in the mediastinal lymph nodes of these patients, no invasive sampling was done. According to the literature, the five-year survival rate for clinical N2 disease is 20% and 30 to 35% for N2 disease confirmed after resection. In previous studies, the five-year survival rate for clinical N2 disease ranges between 10 and 15% and this rate ranges between 25 and 30% for N2 disease confirmed after resection.^[5,6] A considerable number of N2 disorders were clinically identified even at Stage IA, according to a study in the literature.^[7]

In general, direct surgery is recommended for patients with single-station N2 owing to the significant survival advantage over multi-station N2 cases after surgery. In the study of Watanabe et al.,^[6] the five-year survival rate was 35% in single-station N2 and 9% in multi-station N2. Patients with bulky N2 have a very poor prognosis and, therefore, surgery is not recommended.^[8] In our study, the three-year survival rate in single-station N2 cases (n=10, 16.3%) was 60% and the median survival was 27 months. In this group, four of our patients died, while six of them survived. Although the survival rate of N2 patients in our study seems to be better than other N2 patients in the literature, it does not have a significant value due to the small size of our group.

According to studies by Asamura et al.^[7] and Goldstraw et al.,^[9] patients with Stage IIIA had a five-year survival rate of 18% and 33%, respectively. In our study, the five-year survival rate for Stage IIIA disease was 52.5% with a median survival of 42 months. In the subgroups of the 40 Stage IIIA patients in our study, 29 (72.5%) patients were T3N1M0 and T4N0M0. Compared to Stage IIIA cases in the literature, our group had a more homogeneous distribution of subgroups and a better outcome in terms of lymph node metastasis, with fewer lymph node metastases. Therefore, the survival rates are higher in our study.

According to the National Comprehensive Cancer Network (NCCN) 2020 guidelines, direct surgery is not recommended for the Stage IIIB group. In this stage, surgery is indicated in only T3N2 patients according to restaging after neoadjuvant after neoadjuvant treatment.^[10] However, in most cases, the primary operation has no oncological value. Naruke et al.^[11] found a five-year survival of only 8% in a small proportion of operated T4N2 cases. In our study, the three-year survival rate was 71.4% and the median survival was 32 months in Stage IIIB patients (n=7, 11.4%) who underwent surgery. However, these values were not statistically significant due to the small size of our patient group.

Pericardial invasion, pulmonary artery invasion, pulmonary vein invasion, pulmonary artery invasion, pulmonary vein invasion of a centrally located tumor or pulling of the vessels by the tumor make it difficult to clearly identify the location of the vessel dissection area from the hilus. In this case, intrapericardial pneumonectomy becomes inevitable. Considering the studies, limited pericardial invasion and absence of mediastinal lymph node metastasis in this group are among the good prognostic factors. Intrapericardial pneumonectomies for pulmonary artery ligation had the highest survival rates in this group. In a study, the five-year survival rate of intrapericardial pneumonectomy for pulmonary artery invasion was found to be 52.8%.^[2] In our study, 30 (49.2%) patients underwent intrapericardial pneumonectomy and there was no operative mortality. The five-year survival rate was 54.7% and the median survival was 43 months, consistent with previous studies in the literature.

Lung cancers with chest wall involvement are often resectable and surgical treatment is achieved with en bloc resection. In studies, the five-year survival rates with complete resection vary between 15 and 40%. Complete resection, absence of lymph node metastasis, depth and extent of invasion are among the factors affecting survival. McCaughan et al.^[12] reported a five-year survival rate of 48% and Piehler et al.^[13] of 75%. In the absence of lymph node metastasis, the five-year survival rate was reported as 67% in the study by Facciolo et al.^[14] and 49% in the study by Downey et al.^[4] In our study, 21 (24.4%) patients underwent en bloc chest wall resection and there was no operative mortality. The five-year survival rate was found to be 59% and the median survival was 47 months. Our results are consistent with the literature.

Recent studies and advancements in the use of tracheal sleeve pneumonectomy, which is used in patients with carina involvement, have produced positive outcomes. Dartevelle^[15] found a five-year

survival rate of 23% and an operational mortality rate of 11% in a series of 55 patients. According to Roviaro et al.,^[16] the five-year survival rate was 33.4%, while the operational mortality rate was 7.5%. Tastepe et al.^[17] found a mean survival rate of 87 months and a five-year survival rate of 77% in a group of 13 patients. In our study, eight patients underwent tracheal sleeve pneumonectomy and there was no operative mortality. With a median survival of 81 months, the five-year survival rate was 75%. Our findings are consistent with recent findings reported in the literature. We believe that the low rate of tracheal sleeve pneumonectomy mortality rate in our study compared to the studies in the literature is due to the low number of cases compared to the studies in the literature, the absence of additional morbidity in the patients to whom this operation technique would be applied, and the very sensitive selection criteria. In addition, we believe that the use of pedicled autologous grafts such as latissimus dorsi muscle and pericardial adipose tissue contributes to healing by supporting the bronchial stump well and preventing the development of bronchopleural fistula.

Vena cava superior invasion is in the form of direct mass invasion in some cases and only mediastinal structures are involved. Therefore, it is suitable for en bloc resection.^[18] In a study of 14 patients, Dartevelle^[19] reported a five-year survival rate of 31% and a mortality rate of 7%. In their study, Yildizeli et al.^[18] reported a five-year survival rate of 25% and a mortality rate of 12%. One patient in our study had a vena cava superior resection. The patient's 41-month follow-up continues uneventfully. We believe that this situation, which is not frequently encountered, can be applied to isolated tumors by evaluating the cases well. However, due to morbidities and mortality that may occur due to the grafts used after resection, we suggest that a multidisciplinary approach should be followed.

In cases where the tumor directly invades the vertebrae and surrounding tissues, surgical treatment is technically feasible in very few cases. In addition, local regional recurrences are frequently encountered. The lack of sufficient studies in this field makes the effect of this surgical technique on survival questionable. In the study conducted by Gandhi et al.^[20] local recurrences were not detected in patients who received pre- and postoperative radiotherapy. In another study by Rusch et al.,^[21] combined treatment increased resectability and survival time. In our study, one patient underwent vertebral resection. The patient's 57-month follow-up continues uneventfully.

Although technically feasible in a very small number of cases, the survival benefit of vertebral resection is still controversial. However, we believe that patients may be given a chance in the presence of isolated tumors, as in our case.

In carefully selected cases, surgical treatments are used to treat patients with lung cancer-related diaphragmatic invasion. Several studies have shown that if the diaphragmatic invasion is minimal and R0 resection is feasible, surgical resection increases survival.^[2] Yokoi et al.^[22] reported a five-year survival rate of 22.6% in a series of 63 patients following complete resection. The survival of incomplete resections was not reported in the same study. According to this study, the depth of the invasion was the main determinant factor for survival. In our study, diaphragmatic resection was performed in one patient. The 38-month follow-up of the patient continues uneventfully. When the tumor invades the diaphragm in a limited area and is completely removed through resection, as in our case and in the literature, it dramatically increases the chance of survival. We suggest that it is useful to apply this method in selected cases.

Surgery is rarely performed in lung cancers with esophageal involvement. However, due to a lack of appropriate research and a lack of benefit to survival in the studies conducted, this surgical treatment is not usually carried out. During our study, one patient had the muscular layer of the esophagus resected. The patient's 58-month follow-up continues uneventfully. Combined lung and esophageal resection in invasive lung cancers is not preferred very often currently due to high postoperative morbidity and mortality rates and impaired quality of life.

Adjuvant chemotherapy increases the chance of survival in Stage IIIA and Stage IIIB, according to a number of studies.^[23,24] Adjuvant chemotherapy and survival were shown in our study to be statistically significantly correlated (p=0.003). A median survival of 53 months and one-year survival rates of 87.1% and 68%, respectively were seen in patients who underwent postoperative adjuvant chemotherapy. The success of adjuvant chemotherapy in treating micrometastases, that were not preoperatively detectable and in preventing further metastases, accounts for its statistical relevance. Chemotherapy also contributes significantly to survival by preventing local regional recurrences.

Numerous studies have demonstrated the advantages of adjuvant CRT for postoperative

survival. Localized recurrence can be prevented by using adjuvant CRT in the postoperative stage.^[3] When we compared the cases in our study as those who received adjuvant chemotherapy and those who received adjuvant CRT in the postoperative period, the one-year survival rates of the patients who received adjuvant CRT were higher than those who received adjuvant chemotherapy. However, we found that patients who underwent adjuvant chemotherapy had better outcomes based on the five-year survival rates and life expectancy. The median survival time was 53 months in individuals who had adjuvant CRT, and the five-year survival rate was 68%.

In the cases of lung cancer, surgery is the most effective treatment option. The main goal of surgery is to perform resection without leaving tumor cells behind, leaving a clean surgical margin. Locally advanced lung cancers are a heterogeneous group, ranging from Stage IIB (T3N0) tumors to Stage IIIB (T3N2). The survival chances of these cases are increased by the fact that locally advanced cases can still receive surgical treatment and that this surgical treatment involves extended lung resections performed in carefully selected patients.

A comprehensive patient performance evaluation, detailed radiological examinations, preoperative invasive staging methods when necessary, and neoadjuvant chemotherapy or CRT applications have become important in determining candidates suitable for extended lung resection. Extended lung resection in patients receiving neoadjuvant therapy should be planned according to the restaging that would be carried out later.

The limitations of the study are that it is retrospective, single-centered, and the number of cases is not large enough. We believe that multicenter, prospective studies with larger samples will contribute to the researches in this field.

In conclusion, the extended lung resection used to treat locally advanced lung cancer in our clinic was similar to the extended lung resection used in international and domestic clinics. Although it may be daunting for surgeons, intrapericardial pneumonectomy is a technique that should be employed without hesitation, when necessary. It is technically simpler to perform pneumonectomy in selected cases and contributes significantly to survival. Based on these findings, we suggest that extended lung resection should not be ignored in selected cases. **Ethics Committee Approval:** The study protocol was approved by the Karadeniz Technical University Faculty of Medicine Scientific Research Ethics Committee (date: 21.12.2020, no: 2020/333). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Patient Consent for Publication: A written informed consent was obtained from each patient.

Data Sharing Statement: The data of this study were obtained from the patient database of Karadeniz Technical University Faculty of Medicine Farabi Hospital. The data can be shared if the corresponding author is reached via e-mail.

Author Contributions: Have given substantial contributions to the literature search, data collection, study design, analysis of data, manuscript preparation and review of manuscript: O.T., A.T., S.K., A.B.; Analysis interpretation of the data and review of manuscript: O.T., A.T., S.K., C.T.; Revised it critically: O.T., S.K. All authors read and approved the final version of the manuscript.

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REFERENCES

- Crinò L, Weder W, van Meerbeeck J, Felip E; ESMO Guidelines Working Group. Early stage and locally advanced (nonmetastatic) non-small-cell lung cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 2010;21 Suppl 5:v103-15. doi: 10.1093/annonc/mdq207.
- 2. Yaran P, Yazıcı Ü, Taştepe Aİ. Akciğer kanserinde genişletilmiş rezeksiyonlar. J Clin Anal Med 2010:32-40.
- Choi HS, Jeong BK, Jeong H, Lee YH, Ha IB, Song JH, et al. Application of the new 8th TNM staging system for non-small cell lung cancer: Treated with curative concurrent chemoradiotherapy. Radiat Oncol 2017;12:122. doi: 10.1186/ s13014-017-0848-2.
- Downey RJ, Martini N, Rusch VW, Bains MS, Korst RJ, Ginsberg RJ. Extent of chest wall invasion and survival in patients with lung cancer. Ann Thorac Surg 1999;68:188-93. doi: 10.1016/s0003-4975(99)00456-7.
- LoCicero III J. Results of surgical treatment of non-small cell lung cancer. In: Shields TW, editor. 8th ed. General thoracic surgery. Philadelphia: Lippincott Williams & Wilkins; 2018. p. 1222-52.
- 6. Watanabe Y, Hayashi Y, Shimizu J, Oda M, Iwa T. Mediastinal nodal involvement and the prognosis of non-small cell lung cancer. Chest 1991;100:422-8. doi: 10.1378/chest.100.2.422.
- 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;3:46-52. doi: 10.1097/JTO.0b013e31815e8577.
- Martini N, Kris MG, Flehinger BJ, Gralla RJ, Bains MS, Burt ME, et al. Preoperative chemotherapy for stage IIIa (N2) lung cancer: The Sloan-Kettering experience with 136 patients. Ann Thorac Surg 1993;55:1365-74. doi: 10.1016/0003-4975(93)91072-u.

- Goldstraw P, Crowley J, Chansky K, Giroux DJ, Groome PA, Rami-Porta R, et al. The IASLC Lung Cancer Staging Project: Proposals for the revision of the TNM stage groupings in the forthcoming (seventh) edition of the TNM classification of malignant tumours. J Thorac Oncol 2007;2:706-14. doi: 10.1097/JTO.0b013e31812f3c1a.
- Ettinger DS, Wood DE, Aisner DL, Akerley W, Bauman JR, Bharat A, et al. Non-small cell lung cancer, version 3.2022, NCCN clinical practice guidelines in oncology. J Natl Compr Canc Netw 2022;20:497-530. doi: 10.6004/jnccn.2022.0025.
- 11. Naruke T, Goya T, Tsuchiya R, Suemasu K. Prognosis and survival in resected lung carcinoma based on the new international staging system. J Thorac Cardiovasc Surg 1988;96:440-7.
- 12. McCaughan BC, Martini N, Bains MS, McCormack PM. Chest wall invasion in carcinoma of the lung. Therapeutic and prognostic implications. J Thorac Cardiovasc Surg 1985;89:836-41.
- Piehler JM, Pairolero PC, Weiland LH, Offord KP, Payne WS, Bernatz PE. Bronchogenic carcinoma with chest wall invasion: factors affecting survival following en bloc resection. Ann Thorac Surg 1982;34:684-91. doi: 10.1016/ s0003-4975(10)60909-5.
- Facciolo F, Cardillo G, Lopergolo M, Pallone G, Sera F, Martelli M. Chest wall invasion in non-small cell lung carcinoma: a rationale for en bloc resection. J Thorac Cardiovasc Surg 2001;121:649-56. doi: 10.1067/ mtc.2001.112826.
- Dartevelle PG. Herbert Sloan ecture. Extended operations for the treatment of lung cancer. Ann Thorac Surg 1997;63:12-9. doi: 10.1016/s0003-4975(96)01084-3.
- Roviaro G, Vergani C, Maciocco M, Varoli F, Francese M, Despini L. Tracheal sleeve pneumonectomy: Longterm outcome. Lung Cancer 2006;52:105-10. doi: 10.1016/j. lungcan.2005.12.001.
- 17. Taştepe İ, Gezer S, Öz G, Ege T, Gülhan E, Yazıcı Ü, et al. Tracheal sleeve pneumonectomy: An analysis of 13 cases.

Turk Gogus Kalp Dama 2011;19:221-6. doi: 10.5606/tgkdc. dergisi.2011.017.

- 18. Yildizeli B, Dartevelle PG, Fadel E, Mussot S, Chapelier A. Results of primary surgery with T4 non-small cell lung cancer during a 25-year period in a single center: The benefit is worth the risk. Ann Thorac Surg 2008;86:1065-75. doi: 10.1016/j.athoracsur.2008.07.004.
- Dartevelle PG, Chapelier AR, Pastorino U, Corbi P, Lenot B, Cerrina J, et al. Long-term follow-up after prosthetic replacement of the superior vena cava combined with resection of mediastinal-pulmonary malignant tumors. J Thorac Cardiovasc Surg 1991;102:259-65. doi: 10.1016/ S0022-5223(19)36558-4.
- 20. Gandhi S, Walsh GL, Komaki R, Gokaslan ZL, Nesbitt JC, Putnam JB Jr, et al. A multidisciplinary surgical approach to superior sulcus tumors with vertebral invasion. Ann Thorac Surg 1999;68:1778-84. doi: 10.1016/s0003-4975(99)01068-1.
- Rusch VW, Parekh KR, Leon L, Venkatraman E, Bains MS, Downey RJ, et al. Factors determining outcome after surgical resection of T3 and T4 lung cancers of the superior sulcus. J Thorac Cardiovasc Surg 2000;119:1147-53. doi: 10.1067/ mtc.2000.106089.
- 22. Yokoi K, Tsuchiya R, Mori T, Nagai K, Furukawa T, Fujimura S, et al. Results of surgical treatment of lung cancer involving the diaphragm. J Thorac Cardiovasc Surg 2000;120:799-805. doi: 10.1067/mtc.2000.109706.
- 23. Pignon JP, Tribodet H, Scagliotti GV, Douillard JY, Shepherd FA, Stephens RJ, et al. Lung adjuvant cisplatin evaluation: A pooled analysis by the LACE Collaborative Group. J Clin Oncol 2008;26:3552-9. doi: 10.1200/JCO.2007.13.9030.
- 24. Stewart LA, Burdett S, Tierney JF, Pignon J. Surgery and adjuvant chemotherapy (CT) compared to surgery alone in non-small cell lung cancer (NSCLC): A meta-analysis using individual patient data (IPD) from randomized clinical trials (RCT). J Clin Oncol 2007;25(18 Suppl):7552-2. doi: 10.1200/ jco.2007.25.18_suppl.7552.