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Original Article / *Özgün Makale*

Determination of prognostic factors of surgically treated pathological Stage IIIA non-small cell lung cancer

Cerrahi olarak tedavi edilen patolojik Evre IIIa küçük hücreli dışı akciğer kanserinin prognostik faktörlerinin belirlenmesi

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ABSTRACT

Background: This study aims to identify the prognostic factors in Stage IIIA non-small cell lung cancer and to investigate whether there was a significant difference in terms of overall survival and disease-free survival among the subgroups belonging to this disease stage.

Methods: Between January 2010 and December 2018, a total of 144 patients (125 males, 19 females; median age 60 years; range, 41 to 80 years) who were operated for non-small cell lung cancer in our clinic and whose pathological stage was reported as IIIA were retrospectively analyzed. Data including demographic and clinical characteristics of the patients, histopathological diagnosis, the standardized uptake value of the mass on positron emission tomography-computed tomography, tumor diameter, type of surgery, lymph node metastasis status, visceral pleural invasion, and overall and disease-free survival rates were recorded.

Results: The median survival was 39 (range, 27.8 to 46.1) months and the five-year overall survival rate was 28%. The mean tumor diameter was 4.3±2.7 cm. The median disease-free survival was 37 (range, 28.1 to 48.6) months and the five-year disease-free survival rate was 26.9%. In the multivariate analysis, overall survival and disease-free survival in T2N2M0 subgroup were significantly worse than the other subgroups. The other poor prognostic factors of survival were the standardized uptake value of the tumor, pneumonectomy, and histopathological subtypes other than squamous cell carcinoma and adenocarcinoma. Parietal pleural invasion was significantly associated with worse disease-free survival rates.

Conclusion: Our results showed that there may be significant survival differences between subgroups created by tumor histopathology, lymph node invasion and the type of surgery in a heterogeneous lung cancer stage.

Keywords: Non-small cell lung cancer, pathological Stage IIIA, survival, tumor/node/metastasis.

ÖZ

Amaç: Bu çalışmada, Evre IIIA küçük hücreli dışı akciğer kanserinin prognostik faktörleri belirlendi ve bu hastalık evresine ait alt gruplar arasında genel sağkalım ve hastalıksız sağkalım açısından anlamlı bir fark olup olmadığı araştırıldı.

Çalışma planı: Ocak 2010 - Aralık 2018 tarihleri arasında küçük hücreli dışı akciğer kanseri nedeniyle kliniğimizde ameliyat edilen ve patolojik evresi IIIA olarak raporlanan toplam 144 hasta (125 erkek, 19 kadın; medyan yaş 60 yıl; dağılım, 41-80 yıl) çalışmaya dahil edildi. Hastaların demografik ve klinik özellikleri, histopatolojik tanıları, kitlenin pozitron emisyon tomografi-bilgisayarlı tomografide standart tutulum değeri, tümör çapı, cerrahi türü, lenf nodu metastazı durumu, viseral plevral invazyonu ve genel ve hastalıksız sağkalım oranları dahil olmak üzere veriler kaydedildi.

Bulgular: Medyan sağkalım 39 (dağılım, 27.8-46.1) ay ve beş yıllık genel sağkalım oranı %28 idi. Ortalama tümör çapı 4.3±2.7 cm idi. Medyan hastalıksız sağkalım 37 (dağılım, 28.1-48.6) ay ve beş yıllık hastalıksız sağkalım oranı %26.9 idi. Çok değişkenli analizde genel sağkalım ve hastalıksız sağkalım T2N2M0 alt grubunda, diğer alt gruplara kıyasla, anlamlı düzeyde daha kötü idi. Sağkalımın diğer kötü prognostik faktörleri tümörün standart tutulum değeri, pnömonektomi ve skuamöz hücreli karsinom ve adenokarsinom haricindeki histopatolojik alt tipler idi. Parietal plevra invazyonu, daha kötü hastalıksız sağkalım oranları ile anlamlı düzeyde ilişkili idi.

Sonuç: Sonuçlarımız heterojen bir akciğer kanseri evresinde tümör histopatolojisi, lenf nodu invazyonu ve cerrahi türü ile oluşturulan alt gruplar arasında anlamlı sağkalım farkları olabileceğini göstermiştir.

Anahtar sözcükler: Küçük hücreli dışı akciğer kanseri, patolojik evre IIIA, sağkalım, tümör/nodül/metastaz.

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Lung cancer is the leading cause of cancer-related death in both men and women worldwide and non-small cell lung cancer (NSCLC) accounts for 85% of all cases.[1,2] The most important indicator of prognosis in lung cancer is the tumor stage.[3] As the number of studies on lung cancer survival has increased, modifications in the NSCLC staging can be required on a regular basis. Stage IIIA NSCLC according to the current eighth Tumor, Node, Metastasis (TNM) classification accepted in 2017 is highly heterogeneous tumor stage and includes T4N0M0, T3-4N1M0, and T1-2N2M0 subgroups.[4]

In the present study, we aimed to identify the prognostic factors in occult Stage IIIA NSCLC and to investigate whether there was a significant difference in terms of overall survival (OS) and disease-free survival (DFS) among the subgroups belonging to this disease stage.

PATIENTS AND METHODS

In this single-center, retrospective study, medical data of the patients operated with the diagnosis of NSCLC in the Thoracic Surgery Clinic of Medicine Faculty of Gazi University between January 2010 and December 2018 were reviewed. The patients were restaged according to eighth TNM classification[4] and only those with Stage IIIA were included. Routine preoperative blood tests, pulmonary function tests, thoracic computed tomography (CT), and positron emission tomography (PET)-CT were performed for all patients. In addition, advanced lung function capacity tests such as ventilation-perfusion scintigraphy, cardiopulmonary exercise tests, or carbon monoxide diffusion test were performed, if necessary. According to the guidelines, lymph node sampling was performed by endobronchial ultrasound/transbronchial needle aspiration (EBUS-TBNA) or video assisted mediastinoscopy in patients with mediastinal lymphadenopathy, short axis larger than 1 cm on thoracic CT, or increased standard uptake value (SUV) at mediastinal and/or hilar lymph nodes on PET-CT or in those with a central mass and/or large tumor diameter. Pathological staging was used as the inclusion criterion. The patients with positive N2 station confirmed by histopathologically in clinical staging were referred to induction therapy. Patients who received induction therapy and who had neuroendocrine tumor histopathology (i.e., carcinoid tumor, small cell lung cancer, or large cell neuroendocrine carcinoma) and those with missing follow-up data were excluded from the study. In addition, wedge resection and lack of adequate systematic mediastinal lymph node sampling or dissection were used as the exclusion criteria. All patients included in the study were referred to adjuvant therapy. Adjuvant chemoradiation therapy (sequential or concurrent) was recommended for patients with positive N2 stations. Patients who could not tolerate adjuvant therapy due to poor medical status were excluded from the study. Finally, a total of 144 patients (125 males, 19 females; median age 60 years; range, 41 to 80 years) who fulfilled the inclusion criteria were included in the study. The study flow chart is shown in Figure 1.

Data including demographic and clinical characteristics of the patients and operative data (i.e. age, sex, tumor histopathology, tumor diameter, type of surgery, lymph node invasion status, presence of visceral pleural invasion, number and location of metastatic N2 station, SUV on PET-CT and Stage IIIA subgroups [T1N2M0, T2N2M0, T3N1M0, T4N0M0, and T4N1M0]) were recorded. A written informed consent was obtained from each patient. The study protocol was approved by the Medicine Faculty of Gazi University Ethics Committee (Number: 2019-259). The study was conducted in accordance with the principles of the Declaration of Helsinki.

The OS was defined as the length of time from surgery to death or the final follow-up. The DFS was defined as the time from surgery to local recurrence/distant metastasis or follow-up period. The skip lymph node metastasis was defined as lymph node metastasis

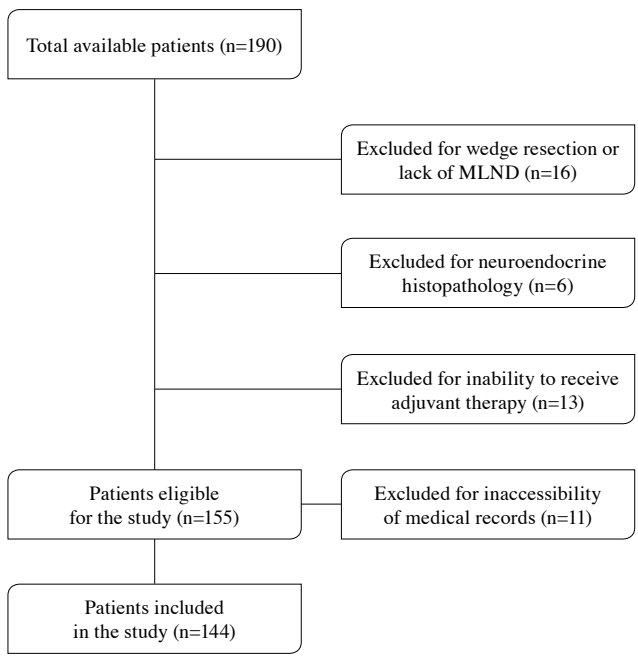

Figure 1. A CONSORT diagram of patient selection.
MLND: Mediastinal lymph node dissection.

directly at N2 stations without metastasis at N1 stations. Each subgroup was compared with each other and the group with the worst OS and DFS rates was compared with all Stage IIIA subgroups.

Statistical analysis

Statistical analysis was performed using the IBM SPSS version 20.0 software (IBM Corp., Armonk, NY, USA). Descriptive data were expressed in mean ± standard deviation (SD), median (min-max) or number and frequency. Chi Square test was used for categorical variables and log rank test was used for continuous variables. The OS was analyzed using the Kaplan-Meier method with 95% confidence interval (CI). Survival differences between the groups were analyzed using the log-rank test or Cox regression analysis. Survival analyses according to SUV of the mass, surgical technique (i.e., lobectomy, pneumonectomy), histopathology, subgroups of Stage IIIA based on multivariate Cox analysis and all analyses were performed in 95% CI. A two-sided p value of <0.05 was considered statistically significant.

RESULTS

The mean tumor diameter was 4.3±2.1 cm. A total of 62 patients (43%) had a left-sided tumor, while 82 patients (57%) had a left-sided tumor. The most common localization was the right upper lobe in 41 patients (28.5%), followed by the left upper lobe in 28 patients (19.4%). A total of 59 patients (40.9%) had various degrees of pleural invasion, while there was no pleural invasion in 85 patients (59.1%). Histopathologically, 69 patients (47.9%) had a squamous cell carcinoma (SCC), 64 patients (44.5%) had an adenocarcinoma (AC), and 11 patients (7.6%) had other tumor types (n=4 large cell carcinoma, n=2 pleomorphic carcinoma, and n=5 adenosquamous cell carcinoma). Lobectomy was performed in 81 (56.2%), pneumonectomy in 41 (28.5%), lung resection with chest wall resection in five (3.5%), bilobectomy in nine (6.3%), and sleeve resection in eight patients (5.5%). Clinicopathological features of the patients and the median OS and DFS rates are summarized in Table 1 and 2, respectively.

The median survival was 39 (range, 27.8 to 46.1) months and the five-year OS rate was 28% (Figure 2). There was no significant difference between the groups in terms of (younger or older than 70 years). According to the TNM subgroups, the best median survival was detected in T3N1M0 subgroup as 48 months and the worst survival was found in T2N2M0 subgroup as 30 months. The five-year OS of T2N2M0 subgroup was 19.9%, indicating a significantly worse OS than all other

Table 1. Clinicopathological characteristics of patients (n=144)

	n	%	Median	Range
Age (year)			60	41-80
Sex				
Male	125	86.8		
Female	19	13.2		
Histopathology				
Squamous cell carcinoma	69	47.9		
Adenocarcinoma	64	44.4		
Pleomorphic carcinoma	2	1.4		
Adenosquamous carcinoma	5	3.5		
Large cell carcinoma	4	2.8		
Stage IIIA subgroups				
T4N0M0	30	20.8		
T3N1M0	16	11.1		
T4N1M0	19	13.2		
T1N2M0	40	27.8		
T2N2M0	39	27.1		
Operation				
Lobectomy	81	56.3		
Pneumonectomy	41	28.5		
Lung resection + CWR	5	3.5		
Bilobectomy	9	6.3		
Sleeve resection	8	5.6		
N status				
N0	30	20.8		
N1	35	24.3		
N2	79	54. 9		
Localization				
Right upper lobe	41	28.5		
Right middle lobe	2	1.4		
Right lower lobe	17	11.8		
Right hilum	22	15.3		
Left upper lobe	28	19.4		
Left lower lobe	15	10.4		
Left hilum	19	13.2		
Pleural invasion				
VPI (+)	50	34.7		
VPI (-)	85	59		
PPI	9	6.3		
N2 distribution (n=79)				
2R	2	2.6		
4R	16	20.3		
3	1	1.2		
7	12	15.1		
9R	1	1.2		
R-multiple	14	17.8		
4L	2	2.6		
5	14	17.8		
6	7	8.8		
9L	2	2.5		
L-multiple	8	10.1		
Skip N2 metastasis	7	8.8		

CWR: Chest wall resection; VPI: Visceral pleural invasion; PPI: Parietal pleural invasion.

Table 2. Survival analyses and p values of patients according to various prognostic factors

Characteristics	n	%	Median survival	Range (month)	*p* value (survival)	Median DFS	Range (month)	*p* value (DFS)
Age (year)								
<70	121	84	43	36.6-49-6	0.12	44	36.3-51.6	0.31
≥70	23	16	29	17.8-39.2		35	21.2-48.3	
TNM factor								
T2N2M0	39	27	26.3	18.3-34.7	0.04	26	18.3-34.4	0.04
Other	105	73	45.7	37.7-53.7		46	37.7-53.7	
SUV of primary lesion on PET/CT								
0-≤3	9	6.3	78	67.7-89.7		70.4	55.2-85.5	
3-≤9	48	33.3	47	37.4-57.3	0.01*	40.1	29.7-50.5	0.01†
>9	87	60.4	32	24.5-38.5		38.0	27.3-48.6	
Histopathology								
SCC-Adenocarcinoma	133	92.4	27	25.6-48.3	0.01	42.1	22.7-50.6	0.64
Other	11	7.6	17	4.8-28.1		36.7	34.9-49.4	
Visceral pleura invasion								
Nil	50	34.7	41	31.6-50.3		40	33.4-46.5	
Yes	85	59.0	33	19.8-46.1	0.54	37	27.0-47.0	0.03
Parietal pleura invasion	9	6.3	24	7.0-40.9		10	4.4-15.5	
Resection								
Pneumonectomy	41	28.4	32	20.7-43.4	0.02	45	30.3-60.7	0.84
Other	103	71.6	45	38.1-51.9		41	33.1-48.7	

DFS: Diseases free survival; TNM: Tumor, node, metastasis; SUV: Standard uptake value; PET-CT: Positron emission tomography-computed tomography; SCC: Squamous cell carcinoma; *, † The diseases free survival and overall survival of the patients with SUV value of primary lesion on PET/CT less than 3 was significantly better than others.

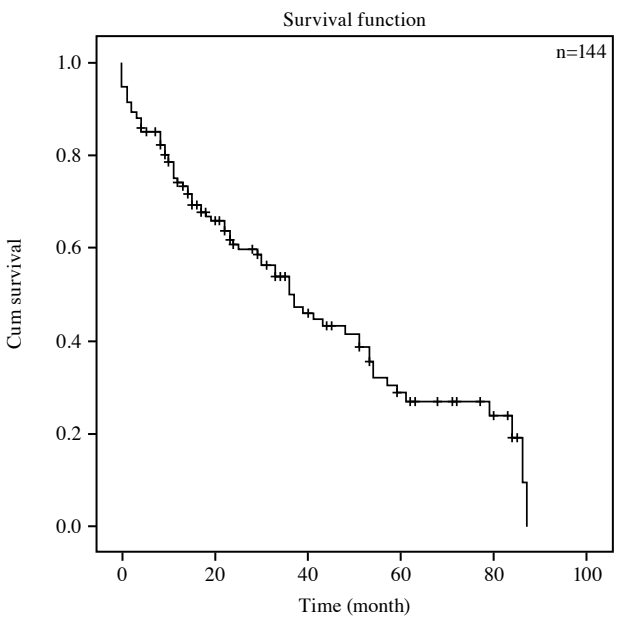

Figure 2. Kaplan-Meier plot of overall survival.

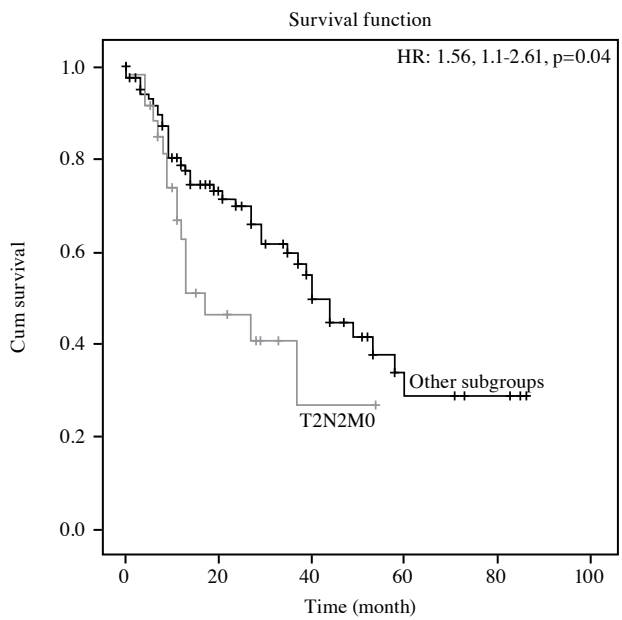

Figure 3. Comparison of T2N2M0 subgroup with other subgroups in terms of overall survival.

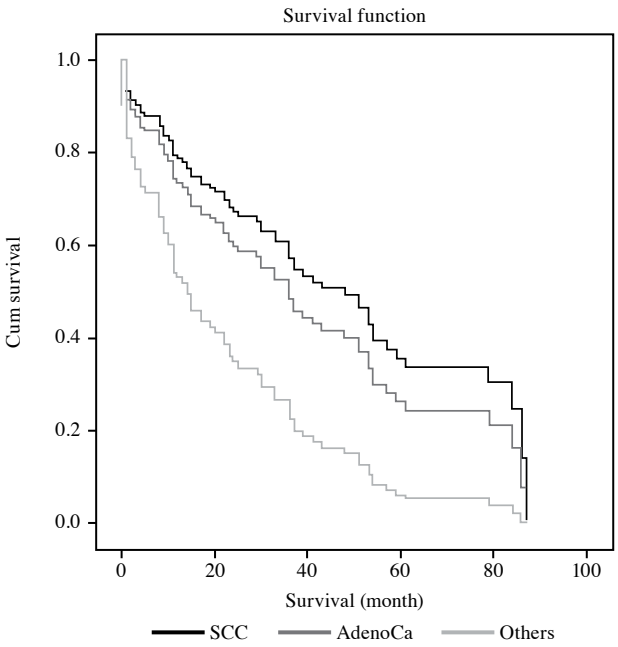

Figure 4. Overal survival comparison according to histopathological subtypes.

SCC: squamous cell carcinoma; AdenoCa: Adenocarcinoma; Others: Large cell carcinoma; Pleomorphic carcinoma: Adenosquamous cell carcinoma.

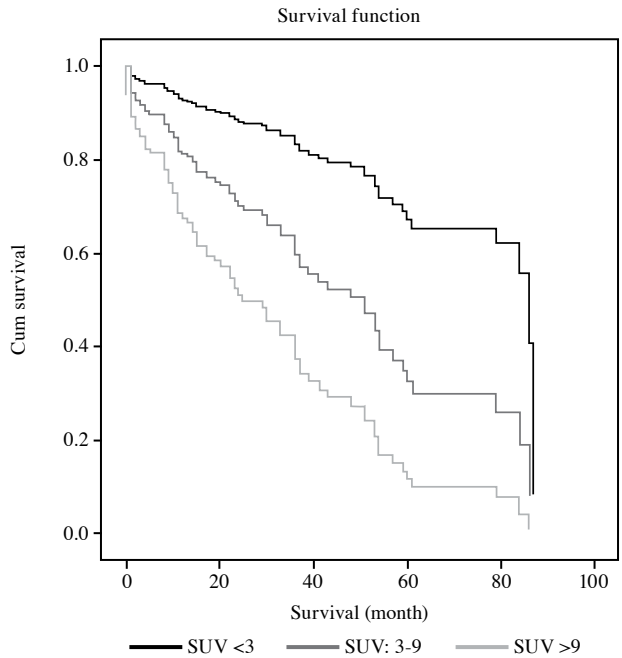

Figure 5. Survival comparison according to SUV (standard uptake value) on PET-CT, p=0.01.

SUV: Standard uptake value; PET-CT: Positron emission tomograph-computed tomography.

subgroups (hazard ratio [HR]: 1.56; 95% CI: 1.1-2.6, p=0.04) (Figure 3). Throughout the study period, there were 29 patients with NSCLC in Stage IIIB operated in our department, and the median survival of these patients was 23 (range, 18.2 to 35.7) months and the five-year OS was 21.2%. The survival of T2N2M0 subgroup was similar to that of Stage IIIB. Histopathologically, the median survival was found as 36 (range, 29.3 to 42.6) months in the AC group, 53 (range, 34 to 66.5) months in the SCC group, and 17 (range, 4.8 to 28.1) months in the other histopathological group, indicating a statistically significant difference (HR: 2.30; 95% CI: 1.1-4.6, p=0.01) (Figure 4).

Table 3. Survival comparison of the T2N2M0 subgroup according the surgical procedure, SUV and tumor histopathology (n=39, multivariate analyze, 95% confidence interval)

Variables	n	%	Median survival (month)	*p*	Hazard ratio (95% CI)
Surgery					
Pneumonectomy	14	35.8	23.7	0.13	0.56 (0.25-1.2)
Other resections	25	64.2	35.8		
SUV (PET-CT)					
3-≤9	12	30.7	33.7	0.80	0.9 (0.39-2.17)
>9	27	69.3	30.8		
Histopathology					
Adenocarcinoma	19	48.7	29.4		
SCC	19	48.7	33.6	0.58	0.7 (0.09-5.5)
Other	1	2.6	29		

TNM: Tumor, node, metastasis; SUV: Standard Uptake Value; CI: Confidence interval; PET-CT: Positron emission tomography-computed tomography; SCC: Squamous cell carcinoma.

The patients were classified according to the SUV on PET-CT, as ≤3, 3 to 9, and >9 and 9 was considered the median uptake value of the study. The median survival was found to be 78 (range, 67.7 to 89.7) months in patients with a SUV of ≤3 and it was found to be significantly higher, compared to other groups (47 months in patients with SUV: 3-9 and 32 months in SUV >9 group; HR: 0.18; 95% CI: 0.06-0.53, p=0.01) (Figure 5). We also analyzed the T2N2M0 subgroup within itself using the PET-SUV value (HR: 0.9, 95% CI, p=0.80), pneumonectomy (HR: 0.5, 95% CI, p=0.13), and histopathological type (HR: 0.7, 95% CI, p=0.58) (Table 3).

In patients with right-sided N2 station metastasis, the best survival was detected in the 2R station-positive group as 39 months and the worst survival was found in multiple N2-positive group as 30 months, although no statistically significant correlation was found (p=0.69). Similarly, there was no significant difference in the survival rates of the patients who had left-side N2 station metastasis based on the number and location of lymph nodes. In the analysis performed according to pleural invasion, the best median survival was found to be 41 (range, 31.6 to 50.3) months in the non-pleural invasion group and the worst survival was found in the parietal pleural invasion group to be 24 (range, 7.0 to 40.9) months, indicating no statistically significant correlation. Tumors with N2 station positivity were classified according to the T status as T1 and T2, and the median survival was 45.5 (range, 33.6 to 57.5) months in the T1 group and 26.3 (range, 18.3 to 34.7) months in the T2 group, indicating a statistically significant difference (HR: 2.1; 95% CI: 1.1-3.9, p=0.03). In addition, T4 tumors were grouped as 7-≤8 cm, 8-≤9 cm and 9-≤10 cm, and >10 cm according to their diameter, and the best median survival was detected in the first group as 45 (range, 16.5 to 73) months and the worst survival was found to be 31 (range, 13.5 to 48.1) months in those whose tumor diameter greater than 10 cm, although there was no statistically significant difference (p=0.09).

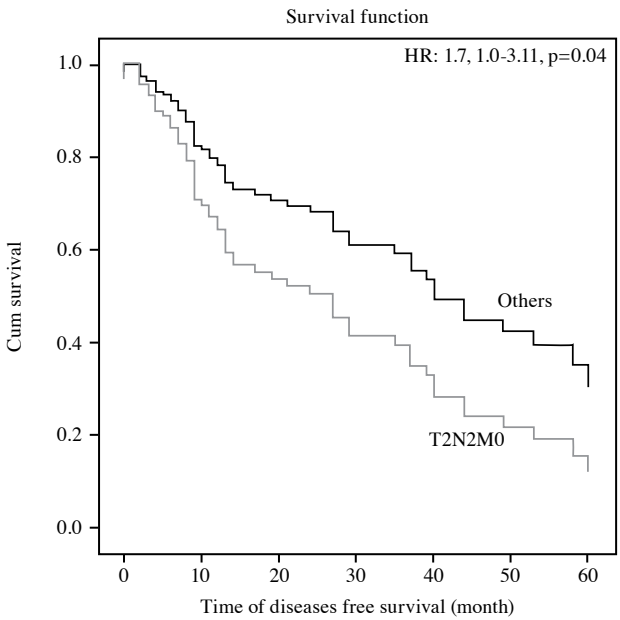

Figure 6. Comparison of T2N2M0 subgroup with other subgroups in terms of disease-free survival.

The median DFS was found to be 37 (range, 28.1 to 48.6) months and the five-year DFS rate was 26.9% for all Stage IIIA patients. Histopathologically, the best DFS was found to be 50.4 (range, 40 to 60.8) months in the SCC group and the worst to be 36.2 (range, 22.7 to 50.6) months in the other histopathological groups; however, it did not statistical significance (p=0.64). The median DFS was found to be better in the pneumonectomy group than the others, although this result was not statistically significant, either. The median DFS was 37 months in the patients with visceral pleural invasion, 40 months in those without pleural invasion, and it was found to be statistically significant worse in patients with parietal pleural invasion (p=0.03).

There was a significant correlation between the DFS and SUV on PET-CT (p=0.02). When the T2N2M0 group and the others were compared, the median DFS was 26 (range, 18.3 to 34.4) months and 46 (range, 37.7 to 53.7) months, respectively, indicating a statistically significant difference (HR: 1.7; 95% CI: 1.0-3.11, p=0.04) (Figure 6). On the other hand, there was no significant difference in DFS rates in single or multiple lymph node station metastases in patients who had a positive N2 station. Skip lymph node metastasis was detected in seven patients in our study. The median survival in N2 patients with skip metastasis was 31 (range, 11.6 to 49.9) months, whereas it was 42 (range, 34.7 to 50.8) months in the patients with N1 and N2 lymph node metastases. However, there was no statistically significant correlation (p=0.33).

DISCUSSION

The first systematic TNM staging in lung cancer has been proposed by Mountain[5] in an article published in 1974. Since then, many major changes have been made and the current eighth TNM staging has been implemented in 2017.[6] As the number of studies investigating the correlation between survival and pathological stage of lung cancers has increased, the

revisions have been made in the TNM classification to reflect prognosis more accurately. According to the eighth TNM classification, Stage IIIA is a highly heterogeneous group which contains five different tumor subgroups, namely T1N2M0, T2N2M0, T3N1M0, T4N1M0, and T4N0M0. Goldstraw et al.[7] reported that a median survival of 41.9 months and a five-year OS rate of 41% in pathological Stage IIIA disease.

There are conflicting studies about the relationship between lung cancer surgery and age in the literature. It has been thought that elastic recoil and pulmonary reserve decreases, comorbidities and surgical mortality increases with aging.[8] However, Aytekin et al.[9] reported that there was no significant difference in the 30-day mortality and five-year survival OS between the groups younger and older than 70 years of age. Dell'Amore et al.,[10] demonstrated satisfactory results in terms of mortality, morbidity, and long-term survival with a careful preoperative evaluation in patients older than 75 years. In contrast, Mery et al.[11] reported that the prognosis of patients older than 65 years was worse than younger with lower median and five-year OS rates. In our study, the median survival was 29 (range, 17.8 to 39.2) months in the patients aged ≥70 years and 43 (range, 36.6 to 49-6) months in the patients younger than 70 years, although we found no significant correlation between the survival rates and age (p=0.12). This result indicates that medical performance status, such as physiological status, respiratory and cardiac capacity, and comorbidities of the patients should be considered rather than the age of patients while planning surgery for lung cancer.

Many authors have proposed that pneumonectomy is a disease in itself and it is an important negative prognostic factor for survival.[12-14] Consistent with the literature, in our study, the median survival of pneumonectomy group was statistically significantly worse than the other surgical types. The relationship between the SUV on PET-CT and survival has been described in many studies in the literature. Okereke et al.[15] reported that SUV was a determinant in both T/N factor and prognosis. Kieninger et al.[16] also suggested that SUV was associated with prognostic indicators such as stage and grade in lung cancer; however, it did not have a prognostic significance by itself. Cistaro et al.[17] found a significant relationship between SUV and DFS in patients with early-stage lung cancer. In our study, the patients were divided into three groups according to the SUV of the primary lesion using PET-CT. The first group had a SUV of ≤3 (hypermetabolic cut-off value), the second group had a SUV of 3-9 (9 was median uptake value of our study), and the third group had a SUV of ≥9. We found a statistically significant difference in the survival rates among these groups. Furthermore, the tumor diameter and lymph node invasion are the factors associated with the tumor stage and these have been reported as poor prognostic factors in a previous study.[18] In our study, the tumor size was a significant prognostic factor for survival consistent with the literature. In order to create homogeneous groups, the classification was made according to the tumor diameter in the same subgroups. When T3 tumors were grouped as 5-6 cm and 6-7 cm according to their diameter, we found a statistically significant correlation between the tumor diameter and OS.

In the literature, there are controversial results regarding DFS in Stage IIIA NSCLC patients. Endo et al.[19] reported a five-year DFS of 25% in Stage IIIA NSCLC patients and significant prognostic factors were visceral pleural invasion and tumor diameter. Choi et al.[20] found the five-year DFS to be 39.6 in these patients and significant prognostic factors for DFS were complete resectability and induction therapy. Tseden-Ish et al.[21] also reported a median survival of 25.1 months in Stage IIIA patients. Similarly, Cerfolio and Bryant[22] found that poor tumor differentiation, multiple N1 station positivity, and lack of adjuvant therapy were the main poor prognostic factors for DFS in Stage IIIA NSCLC patients. In our study, the median DFS was found 37 (range, 21.5 to 58.4) months and five-year DFS rate was 26.9%. Significantly poor prognostic factors for DFS included parietal pleural invasion, high SUV on PET-CT, and T2N2M0 subgroup. The median DFS was found to be 37 months in the presence of visceral pleural invasion, 40 months in those without pleural invasion, and 10 months in patients with parietal pleural invasion (p=0.03). The median DFS was 70.4 (range, 55.2 to 85.5) months and 39.8 (range, 30.2 to 49.5) months in the group with SUV <3 and SUV> 9 on PET-CT, respectively (p=0.02). In addition, it was 37 (range, 22.9 to 51) months in the T1N2M0 group and 26 (range, 18.3 to 34.4) months in the T2N2 group (p=0.03). Although not statistically significant, other factors which affected DFS were other histopathologies and surgery except than pneumonectomy. In our study, the occult N2 ratio was higher than the literature. In N2 staging, we applied the European Society of Thoracic Surgeon (ESTS) guidelines. Our pN2 ratio was found to be higher, particularly in patients with AC, and a peripheral, small diameter mass without mediastinal involvement on PET-CT. Meanwhile, 749 patients

were operated (i.e., lung anatomic resection and systematic lymph node dissection) with the primary NSCLC diagnosis without receiving neoadjuvant therapy. The occult N2 ratio of our study was found to be 13.4%.

The main limitations of this study are its single-center and retrospective design with a small sample size. In addition, invasive mediastinal staging was unable to be performed in all cases (i.e., peripheral tumor location, tumors with small diameter, the small mediastinal lymph nodes on thoracic CT and no mediastinal involvement on PET-CT).

In conclusion, according to the eighth tumor, node, metastasis, Stage IIIA non-small cell lung cancers are highly heterogenous malignancies. In our study, T2N2M0 group had a significantly worse prognosis compared to other groups in terms of overall survival and disease-free survival. Other significant poor prognostic factors for overall survival and disease-free survival included the tumor diameter, high standard uptake value value on positron emission tomography-computed tomography, other histopathological subtypes (i.e., pleomorphic carcinoma, large cell carcinoma, and adeno-squamous cell carcinoma) and parietal pleural invasion. Nonetheless, further multi-center, large-scale, long-term, prospective studies including T2N2M0 patients are required to obtain a more accurate conclusion.

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