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ORIGINAL ARTICLE / ÖZGÜN MAKALE

# Survival analysis between single-factor and multi-factor groups in Stage T3N0M0 non-small cell lung cancer

*Evre T3N0M0 küçük hücreli dışı akciğer kanserinde tek faktörlü ve çok faktörlü gruplar arasındaki sağkalım analizi*

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## ABSTRACT

***Background:*** This study aims to identify prognostic factors in operated patients with non-small cell lung cancer staged as T3N0M0 according to the 8th edition of the Tumor, Node, Metastasis (TNM) staging system.

***Methods:*** Between January 2010 and June 2023, a total of 79 patients (67 males, 12 females; mean age: 62.9±8.7; range, 40 to 80 years) who underwent surgery for non-small cell lung cancer and were pathologically staged as T3N0M0 were retrospectively analyzed. The patients were divided into two groups: the first group included 56 patients with a single T3 factor, while the second group included 23 patients with multiple T3 factors. Survival analysis was performed.

***Results:*** The five-year overall survival rate for the first group was 79.0%, with a mean overall survival of 107.76±8.44 months (95% confidence interval [CI]: 91.21-124.32), while the second group had a five-year overall survival rate of 48.9%, with a mean overall survival of 69.19±12.60 months (95% CI: 44.48-93.91). This difference was statistically significant (p=0.02). In the multivariate analysis, multiple T3 factors (p=0.003) and the presence of comorbidity (p=0.004) were found to be independent poor prognostic factors.

***Conclusion:*** Our study results suggest that having multiple T factors significantly and adversely affect survival of patients with surgically treated pT3 non-small cell lung cancer.

***Keywords:*** Non-small cell lung cancer, T3, TNM staging, overall survival.

## ÖZ

***Amaç:*** Bu çalışmada küçük hücreli dışı akciğer kanseri nedeniyle ameliyat edilen, Tümör, Nod, Metastaz (TNM) evreleme sisteminin 8. baskısına göre T3N0M0 olarak evrelenen hastalarda prognostik faktörler belirlendi.

***Çalışma planı:*** Ocak 2010 - Haziran 2023 tarihleri arasında, küçük hücreli dışı akciğer kanseri nedeniyle ameliyat edilen ve patolojik evrelemesi T3N0M0 olan toplam 79 hasta (67 erkek, 12 kadın; ort. yaş: 62.9±8.7; dağılım, 40-80 yıl) retrospektif olarak incelendi. Hastalar iki gruba ayrıldı: birinci grup tek bir T3 faktörüne sahip 56 hastadan oluşurken, ikinci grup birden çok T3 faktörüne sahip 23 hastadan oluşuyordu. Sağkalım analizi yapıldı.

***Bulgular:*** Birinci grubun beş yıllık genel sağkalımı %79.0, ortalama genel sağkalımı 107.76±8.44 (%95 güven aralığı [GA]: 91.21-124.32) ay iken, ikinci grubun beş yıllık genel sağkalımı %48.9, ortalama genel sağkalımı 69.19±12.60 (%95 GA: 44.48-93.91) ay idi. Bu fark, istatistiksel olarak anlamlı idi (p=0.02). Çok değişkenli analizde birden fazla T3 faktörünün (p=0.003) ve komorbidite varlığının (p=0.004) bağımsız kötü prognostik faktörler olduğu görüldü.

***Sonuç:*** Çalışma sonuçlarımız, birden fazla T faktörüne sahip olmanın cerrahi olarak tedavi edilen pT3 küçük hücreli dışı akciğer kanseri olan hastaların sağkalımını anlamlı ve olumsuz düzeyde etkilediğini göstermektedir.

***Anahtar sözcükler:*** Küçük hücreli dışı akciğer kanseri, T3, TNM evreleme, genel sağkalım.

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Lung cancer is the leading cause of cancer-related deaths worldwide, and histopathologically, the majority of cases are non-small cell lung cancer (NSCLC). According to the 8th edition of the American Joint Committee on Cancer (AJCC) staging guidelines, the T3 tumor group is a heterogeneous category, defined as tumors with at least one of the following characteristics: tumor size >5 cm, but ≤7 cm satellite nodule (SN) in the same lobe (SN), invasion of the parietal pleura (PPI), invasion of the parietal pericardium, invasion of the chest wall, or invasion of the phrenic nerve. In NSCLC patients with T3 tumor staging, N0 lymph node staging, and M0 metastasis s0taging, the cancer is classified as Stage IIB, representing less than 5% of the operable NSCLC patient group.[1] No changes to the T factor is planned in the 9th edition of the International Association for the Study of Lung Cancer (IASLC) lung cancer staging project.[2,3] The current NCCN guideline (v. 3.2025) recommends surgical total excision and adjuvant chemotherapy for T3N0 disease, excluding superior sulcus tumors.[4]

Several studies have shown the prognostic impact of age, tumor size, and complete resection in T3N0M0 tumors, and recent research has focused on the negative prognostic effect of chest wall invasion and the positive prognostic effect of SNs in the same lobe.[5-8] However, studies on the prognostic impact of multiple T3 factors still remain limited. In the present study, we aimed to investigate the oncological synergistic and prognostic impact of having multiple T3 factors in Stage T3N0M0 NSCLC tumors.

## PATIENTS AND METHODS

This single-center, retrospective study was conducted at Gazi University Faculty of Medicine, Department of Thoracic Surgery between January 2010 and June 2023. Patients whose tumor stage was pT3-pN0 according to 8th edition of the AJCC Tumor, Node, Metastasis (TNM) and who underwent anatomic lung resection (segmentectomy, lobectomy, bilobectomy or pneumonectomy with mediastinal lymph node dissection) were included. Patients with metastatic disease, those receiving neoadjuvant therapy, those with mediastinal or hilar lymph node metastasis, wedge resection, and those with inaccessible records were excluded. Finally, a total of 79 patients (67 males, 12 females; mean age: 62.9±8.7; range, 40 to 80 years) who met the inclusion criteria were enrolled. A written informed consent was obtained from each patient. The study protocol was approved by the Gazi University Ethics Committee (date: 27.02.2024, no: 2024-322). The study was conducted in accordance with the principles of the Declaration of Helsinki.

The patients were evaluated with routine physical examination, chest X-ray, complete blood count, blood biochemistry tests, pulmonary function test, thoracic computed tomography (CT), and positron emission tomography (PET). The preoperative mediastinal staging was performed using PET/CT, endobronchial ultrasound (EBUS), or mediastinoscopy.

The patients were classified according to the 8th edition of the AJCC TNM staging factors for T3 tumors. Two groups were formed: single T3 factors (n=56) and multiple T3 factors (n=23). The single T3 group included only one of the T3 tumor features (tumor diameter, invasion, or SN), whereas the multiple T3 factor group included two or more T3 features.

Data including age, sex, comorbidities, surgical procedures, types of operations, and postoperative treatments were recorded. Pathological data were analyzed based on histopathological type, tumor diameter, surgical margin status, spread through air spaces (STAS), visceral pleura invasion (VPI), PPI, and SN. A distinct pathological classification for rib and intercostal invasion was not defined and both were categorized under PPI.

### Statistical analysis

Statistical analysis was performed using the IBM SPSS version 26.0 software (IBM Corp., Armonk, NY, USA). The conformity of the data to normal distribution was assessed using the Kolmogorov-Smirnov test. Descriptive data were presented in mean ± standard deviation (SD), median and interquartile range (IQR) or number and frequency, where applicable. The overall survival (OS) was defined as the period in months from the surgery date to the date of death for deceased patients and from the surgery date to the study date for living patients. The Kaplan-Meier method was used to estimate the survival probabilities, and the survival differences were compared using the log-rank test. The Cox regression model was used for univariate and multivariate analyses. Hazard ratios (HRs) with 95% confidence intervals (CIs) were provided. A $p$ value of <0.05 was considered statistically significant.

## RESULTS

Of a total of 79 patients, 64 (81.0%) underwent thoracotomy. Chest wall resection was performed in 19 (24.1%) patients, with a median number of ribs resected being 2 (range, 2 to 5). The median tumor diameter was 5.5 (range, 1.3 to 7.0) cm. The most frequent tumor histopathology was squamous cell carcinoma in 36 (45.6%) patients. An SN was present

**Table 1. Baseline demographic and clinical characteristics of patients**

| Variables | n | % | Mean±SD | Median | Min-Max |
|---|---|---|---|---|---|
| Age (year) | | | | | |
| <65 | 45 | 57.0 | 62.9±8.7 | | |
| ≥65 | 34 | 43.0 | | | |
| Number of resected ribs | | | | 2 | 2-5 |
| Tumor diameter (cm) | | | | 5.5 | 1.3-7 |
| Sex | | | | | |
| Male | 67 | 84.8 | | | |
| Female | 12 | 15.2 | | | |
| Comorbidity | | | | | |
| Yes | 48 | 60.8 | | | |
| No | 31 | 39.2 | | | |
| History of tobacco use | | | | | |
| Yes | 69 | 87.3 | | | |
| No | 10 | 12.7 | | | |
| Type of resection | | | | | |
| Segmentectomy | 4 | 5.1 | | | |
| Lobectomy | 53 | 67.1 | | | |
| Sleeve lobectomy | 3 | 3.8 | | | |
| Pneumonectomy | 10 | 12.7 | | | |
| Surgical approach | | | | | |
| Video assisted thoracoscopic surgery | 10 | 12.7 | | | |
| Thoracotomy | 64 | 81.0 | | | |
| Shaw-Paulson | 5 | 6.3 | | | |
| Tumor location | | | | | |
| Right upper lobe | 37 | 46.8 | | | |
| Right middle lobe | 2 | 2.5 | | | |
| Right lower lobe | 12 | 15.2 | | | |
| Right hilar | 1 | 1.3 | | | |
| Left upper lobe | 13 | 16.5 | | | |
| Left lower lobe | 11 | 13.9 | | | |
| Left hilar | 3 | 3.8 | | | |
| Chest wall resection | | | | | |
| Yes | 19 | 24.1 | | | |
| No | 60 | 75.9 | | | |
| Histopathology | | | | | |
| Squamous cell carcinoma | 36 | 45.6 | | | |
| Adenocarcinoma | 31 | 39.2 | | | |
| Pleomorphic carcinoma | 5 | 6.3 | | | |
| Adenosquamous carcinoma | 2 | 2.5 | | | |
| Carcinoid tumor | 2 | 2.5 | | | |
| Mucoepidermoid carcinoma | 1 | 1.3 | | | |
| Large cell neuroendocrine carcinoma | 1 | 1.3 | | | |
| Large cell carcinoma | 1 | 1.3 | | | |
| Visceral pleura invasion | | | | | |
| Yes | 42 | 53.2 | | | |
| No | 37 | 46.8 | | | |
| Parietal pleura invasion | | | | | |
| Yes | 25 | 31.6 | | | |
| No | 54 | 68.4 | | | |
| Spread through air spaces | | | | | |
| Yes | 10 | 12.7 | | | |
| No | 69 | 87.3 | | | |
| Satellite nodule | | | | | |
| Yes | 16 | 20.3 | | | |
| No | 63 | 79.7 | | | |
| Surgical margins | | | | | |
| R0 resection | 68 | 86.1 | | | |
| R1 resection | 11 | 13.9 | | | |
| Adjuvant therapy | | | | | |
| Chemotherapy | 53 | 67.1 | | | |
| Chemoradiotherapy | 9 | 11.4 | | | |
| No | 17 | 21.5 | | | |

SD: Standard deviation.

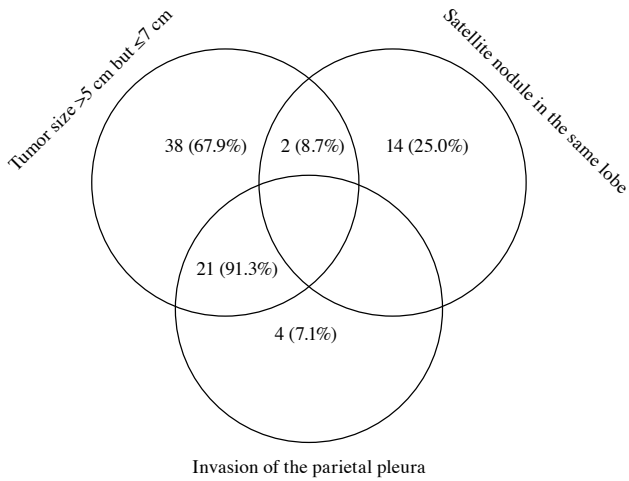



**Figure 1.** Schematic representation of T factor characteristics in single-factor and multiple-factor patient groups.

in 16 (20.3%) patients and PPI in 25 (31.6%) patients. The surgical margin was considered R1 resection in 11 (13.9%) patients. Postoperatively, 53 (67.1%) patients received chemotherapy, and nine (16.5%) received chemoradiotherapy. The demographic, histopathological, and surgical characteristics of the patients are presented in Table 1.

According to the subgroup analysis, 56 (70.9%) patients had a single factor, while 23 (29.1%) had multiple factors. In the single-factor group, 38 (67.9%) patients had the tumor diameter criterion, 14 (25.0%) had an SN, and four (7.1%) had PPI. Among the multiple-factor group, 21 (91.3%) patients had both the tumor diameter criterion and PPI and two (8.7%) had the tumor diameter criterion accompanied by the presence of an SN (Figure 1). Comorbidities were present in 35 (62.5%) patients. Thirteen (56.5%) patients with multiple factors had also comorbidities. In the single-factor group, lobectomy was performed in 44 (78.6%) patients. Chest wall resection was performed in two (3.6%) patients. In the multiple-factor group, lobectomy was performed in 18 (78.2%) patients. Chest wall resection was performed in 17 (73.9%) patients.

The mean tumor diameter in patients with a single factor was 5.11±1.62 cm. Among them, 26 (46.4%) patients had squamous cell carcinoma and 20 (35.7%) patients had adenocarcinoma. Surgical margin assessment showed that six (10.7%) patients had R1 resection. Also, PPI was seen in four (7.1%) patients and SN in 14 (25.0%) patients.

The mean tumor diameter in patients with multiple factors was 5.67±1.31 cm. Among these patients, 10 (43.5%) had squamous cell carcinoma and 11 (47.8%) had adenocarcinoma. Surgical margin assessment showed that five (21.7%) patients had R1 resection. Also, PPI was seen in 21 (91.3%) patients. A satellite nodule was present in two (8.7%) patients. The demographic, histopathological, and surgical characteristics of both groups are presented in Table 2.

The median follow-up period was 56.4 (range, 0 to 150) months. For patients with a single factor, the five-year OS rate was 79.0%, with a mean OS of 107.76±8.44 months (95% CI: 91.21-124.32). In contrast, the five-year OS rate for patients with multiple factors was 48.9%, with a mean OS of 69.19±12.60 months (95% CI: 44.48-93.91) (p=0.02, Figure 2).

In the univariate and multivariate analyses, age, sex, tumor pathology (adenocarcinoma/squamous cell carcinoma/other), SN, PPI, having multiple T3 factors, resection margin (positive/negative), adjuvant therapy, and comorbidity were evaluated. In the univariate analysis, having multiple T3 factors (p=0.027), PPI (p=0.024), and the presence of comorbidity (p=0.050) were identified as significant poor prognostic factors. In contrast, age, sex, tumor pathology (adenocarcinoma/squamous cell carcinoma/other), SN, the presence of complete resection, and adjuvant therapy had no significant effect on prognosis (p>0.05). In the multivariate analysis, only having multiple T3 factors (p=0.003) and the presence of comorbidity (p=0.004) were defined as independent prognostic factors (Table 3).

## DISCUSSION

In the present study, we investigated the oncological synergistic and prognostic impact of having multiple T3 factors in Stage T3N0M0 NSCLC tumors. Our study results showed that the synergistic effect of multiple T factors had a significant negative prognostic impact on survival. Staging in lung cancer is an essential parameter for guiding treatment and predicting prognosis, and it has been continuously refined.[9] In the 8th edition of lung cancer staging guidelines, T3 tumors represent a heterogeneous group, and no changes have been made in this group in the 9th edition.[2,3] Most studies focus on subgroup analyses of T3 factors, while studies on the prognostic impact of multiple factors still remain limited. In studies with inconsistent patient demographics, factors such as age, completeness of resection, tumor size, adjuvant treatments, and depth of invasion have been suggested as prognostic factors.[10-12]

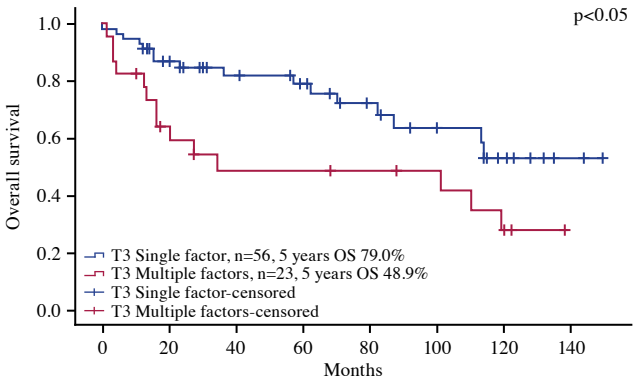
Marques et al.[5] conducted a study including 280 patients with Stage T3N0M0 NSCLC and

**Table 2. Subgroup analyses of single or multiple T3 factors**

| | Single-factor patient group | | | Multiple-factor patient group | | | |
|---|---|---|---|---|---|---|---|
| Variables | n | % | Mean±SD | n | % | Mean±SD | *p* |
| Age (year) | | | 62.3±8.7 | | | 64.3±8.9 | 0.41 |
| Sex | | | | | | | 0.16 |
| Male | 45 | 80.4 | | 22 | 95.7 | | |
| Female | 11 | 19.6 | | 1 | 4.3 | | |
| History of tobacco use | | | | | | | 0.18 |
| Yes | 49 | 87.5 | | 20 | 87.0 | | |
| No | 7 | 12.5 | | 3 | 13.0 | | |
| Comorbidity | | | | | | | 0.81 |
| Yes | 35 | 62.5 | | 13 | 56.5 | | |
| No | 21 | 37.5 | | 10 | 43.5 | | |
| Surgical approach | | | | | | | 0.15 |
| Video assisted thoracoscopic surgery | 9 | 16.1 | | 1 | 4.3 | | |
| Thoracotomy | 47 | 83.9 | | 17 | 73.9 | | |
| Shaw-Paulson | 0 | 0.0 | | 5 | 21.7 | | |
| Type of resection | | | | | | | 0.48 |
| Segmentectomy | 3 | 5.4 | | 1 | 4.3 | | |
| Lobectomy | 44 | 78.6 | | 18 | 78.2 | | |
| Sleeve lobectomy | 3 | 5.4 | | 0 | 0.0 | | |
| Pneumonectomy | 6 | 10.7 | | 4 | 17.4 | | |
| Chest wall resection | | | | | | | **<0.001** |
| Yes | 2 | 3.6 | | 17 | 73.9 | | |
| No | 54 | 96.4 | | 6 | 26.1 | | |
| Tumor diameter (cm) | | | 5.11±1.62 | | | 5.67±1.31 | 0.15 |
| Histopathology | | | | | | | 0.46 |
| Squamous cell carcinoma | 26 | 46.4 | | 10 | 43.5 | | |
| Adenocarcinoma | 20 | 35.7 | | 11 | 47.8 | | |
| Others | 10 | 17.9 | | 2 | 8.4 | | |
| Surgical margins | | | | | | | 0.19 |
| R0 resection | 50 | 89.3 | | 18 | 78.3 | | |
| R1 resection | 6 | 10.7 | | 5 | 21.7 | | |
| Spread through air spaces | | | | | | | 0.49 |
| Yes | 8 | 14.3 | | 2 | 8.7 | | |
| No | 48 | 85.7 | | 21 | 91.3 | | |
| Visceral pleura invasion | | | | | | | **<0.001** |
| Yes | 20 | 35.7 | | 22 | 95.7 | | |
| No | 36 | 64.3 | | 1 | 4.3 | | |
| Parietal pleura invasion | | | | | | | **<0.001** |
| Yes | 4 | 7.1 | | 21 | 91.3 | | |
| No | 52 | 92.9 | | 2 | 8.7 | | |
| Satellite nodule | | | | | | | 0.10 |
| Yes | 14 | 25.0 | | 2 | 8.7 | | |
| No | 42 | 75.0 | | 21 | 91.3 | | |

SD: Standard deviation.

found that chest wall invasion was an independent poor prognostic factor for both OS (HR=2.45, 95% CI: 1.36-4.44, p=0.003) and disease-free survival (HR=3.13, 95% CI: 1.79-5.47, p<0.001) using the multivariate analysis. They also showed that patients with chest wall invasion whose tumors were larger than 5 cm had a worse prognosis than others. Wu et al.[13] analyzed the prognostic effects of PPI and rib




| At risk (year) | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|---|---|
| T3 single factor | 56 | 52 | 35 | 31 | 29 | 25 | 20 | 15 |
| T3 multiple factors | 23 | 18 | 12 | 9 | 9 | 9 | 8 | 8 |

**Figure 2.** Graphical representation and comparison of overall survival analysis between single-factor and multiple-factor patient groups.
OS: Overall survival.

invasion in 8,681 NSCLC patients who underwent surgery. The best OS was observed in those without rib invasion, while the lowest OS was in those with rib invasion. Among patients with isolated PPI, OS was significantly worse for tumors >5 cm. However, in rib invasion cases, tumor size did not affect OS. Patients with tumors >5 cm and PPI had worse survival than those with pT3 classification, but showed no difference from pT4. This study suggests that patients with tumor size >5 cm and parietal pleura invasion should be classified as pT4. Since the poor prognostic impact of rib invasion has been previously reported in the literature, we believe that the poor OS observed in patients with isolated PPI and tumor size >5 cm in this study is valuable in demonstrating the detrimental synergistic effect of tumor size. In the present study, PPI significantly negatively affected OS in the univariate analysis. Among the patient group with PPI, 84.0% had tumors larger than 5 cm. In line with the literature, we believe that the significant decrease in survival in the PPI group is due to the synergistic effect of tumor size.

Komiya et al.[14] analyzed 9,931 Stage T3N0M0R0 NSCLC patients who underwent surgery based on T3 factors. Of these, 8,955 patients were classified as T3 due to a single factor (T3-single), and 884 patients were classified as T3 due to a combination of tumor size (5 cm < tumor size ≤7 cm) and another additional factor (T3-multi). In the OS analysis, the median survival in the T3-multi group was 37.3 months, whereas, in the T3-single group, it was 69.3 months, with the T3-multi group showing statistically significantly worse OS. In multivariate analysis, younger age, female sex, and multi-agent chemotherapy were also found to be associated with longer survival. The authors suggest that the T3 tumor group with multiple factors should be considered for further subgroup analysis, similar to T4 tumors. However, the limitations to this study include the lack of specific T3 descriptors in the database, such as chest wall invasion, pericardial invasion, and additional tumor nodules in the same lobe. As in this study, our T3 multiple group was based on the combination of other T3 factors with tumor size. However, due to our smaller sample size, histopathological and surgical characteristics were more clearly defined.

**Table 3. Results of univariate and multivariate analyses based on some covariates**

| | Univariate | | | Multivariate | | |
|---|---|---|---|---|---|---|
| Variables | HR | 95% CI | *p* | HR | 95% CI | *p* |
| Age ≥65 | 1.569 | 0.762-3.232 | 0.222 | 1.878 | 0.778-4.534 | 0.161 |
| Male | 1.279 | 0.446-3.670 | 0.647 | 1.147 | 0.348-3.780 | 0.821 |
| Histology: Squamous carcinoma *vs*. adenocarcinoma | 1.745 | 0.782-3.894 | 0.174 | 1.537 | 0.603-3.921 | 0.368 |
| Histology: Other *vs*. adenocarcinoma | 0.689 | 0.196-2.419 | 0.561 | 0.956 | 0.247-3.697 | 0.947 |
| Parietal pleura invasion | 2.279 | 1.112-4.670 | 0.024 | 3.849 | 0.819-18.081 | 0.088 |
| Satellite nodule | 0.920 | 0.352-2.406 | 0.866 | 0.726 | 0.221-2.378 | 0.597 |
| Multiple T3 factors | 2.259 | 1.099-4.643 | 0.027 | 7.738 | 2.040-29.348 | 0.003 |
| Incomplete resection | 1.571 | 0.639-3.858 | 0.325 | 2.748 | 0.980-7.710 | 0.055 |
| Comorbidities | 2.107 | 1.000-4.439 | 0.050 | 3.755 | 1.542-9.142 | 0.004 |
| Adjuvant therapy | 0.920 | 0.394-2.147 | 0.848 | 0.978 | 0.382-2.503 | 0.963 |

HR: Hazard ratio; CI: Confidence interval.

In another study, which included 28,519 patients with T3N0-3M0 NSCLC, Cai et al.[15] formed four distinct groups according to the tumor size >5 cm and ≤7 cm (T-size) (n=17,971), chest wall, pericardium, and phrenic nerve invasion (T-invasion) (n=3,028), SNs in the same lobe (T-add) (n=4,600), and multiple T3 factors (T-multiple) (n=2,920). In the OS analysis, the five-year survival rates were 23.3% for T-size, 26.9% for T-invasion, 35.4% for T-add, and 21.5% for T-multiple, with the best OS seen in the T-add group and the worst survival in the T-multiple group. In the multivariate analysis of the pathological N0 group, the T-multiple group had the worst OS (HR=1.377, 95% CI: 1.269-1.495) and cancer-specific survival (HR=1.422, 95% CI: 1.281-1.578), while the T-add group had the best OS (HR=0.803, 95% CI: 0.741-0.869) and cancer-specific survival (HR=0.637, 95% CI: 0.569-0.714; p<0.001). The authors suggest that the T-add and T-multiple factors, with the best and worst prognoses, respectively, should be reclassified in the T staging system. However, the limitations to this study include the inability to access data on surgical margins, genetic mutations, recurrence times, and other parameters, as the study used a national database.

In the current study, when we classified our patient group based on T3 factors, into those with a single factor and those with an additional factor alongside tumor size, we found that the group with multiple factors had a significantly worse OS. We believe that non-size T3 factors, when present along with size, have a synergistic effect on OS and should be considered poor prognostic factors. However, in our group with multiple factors, the number of patients with SNs in the same lobe was too small to allow for a subgroup analysis. Additionally, there was no data on phrenic nerve invasion or parietal pericardial invasion, as these factors were absent. Further studies are needed to assess the synergistic effects of non-size factors with size.

Nonetheless, the present study has some limitations. The first is the inherent limitations associated with its retrospective nature. The second limitation is that it was a single-center study with a relatively small sample size. The third limitation is the inability to standardize and obtain detailed dose information for adjuvant therapy, as some patients received their treatment at other centers; thus, they were only classified as having received treatment or not. Another limitation is the utilization of OS analysis rather than cancer-specific survival analysis.

In conclusion, our study results suggest that having multiple T factors significantly and adversely affect survival of patients with surgically treated pT3 non-small cell lung cancer. Further multi-center, large-scale, prospective studies are warranted to draw more reliable conclusions on this subject.

**Data Sharing Statement:** The data that support the findings of this study are available from the corresponding author upon reasonable request.

**Author Contributions:** Idea/concept, design, control/supervision: İ.T., M.S., Ş.M.D., A.Ç., İ.C.K., A.İ.T., O.K.A.; Data collection and/or processing: İ.T., M.S., Ş.M.D.; Analysis and/or interpretation: İ.T., İ.C.K., A.İ.T.; Literature review: İ.T., M.S., A.Ç., O.K.A.; Writing the article: İ.T., M.S., A.Ç.; Critical review: İ.T., M.S., O.K.A.; References and funding acquisition: İ.T., İ.C.K., O.K.A.; Materials: İ.T., Ş.M.D., A.Ç., İ.C.K.; Other: İ.T., M.S., A.İ.T.

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## REFERENCES

1. Scott WJ, Howington J, Movsas B, American College of Chest P. Treatment of stage II non-small cell lung cancer. Chest 2003;123:188S-201. doi: 10.1378/chest.123.1_suppl.188s.
2. Rami-Porta R, Nishimura KK, Giroux DJ, Detterbeck F, Cardillo G, Edwards JG, et al. The International Association for the Study of Lung Cancer Lung Cancer Staging Project: Proposals for Revision of the TNM Stage Groups in the Forthcoming (Ninth) Edition of the TNM Classification for Lung Cancer. J Thorac Oncol 2024;19:1007-27. doi: 10.1016/j.jtho.2024.02.011.
3. Detterbeck FC, Woodard GA, Bader AS, Dacic S, Grant MJ, Park HS, et al. The Proposed Ninth Edition TNM Classification of Lung Cancer. Chest 2024;166:882-95. doi: 10.1016/j.chest.2024.05.026.
4. Non-Small Cell Lung Cancer: National Comprehensive Cancer Network; 2025 [cited Version 3.2025].
5. Marques E, Kennedy KF, Giroux DJ, Cilento VB, Nishimura KK, Fang W, et al. Oncologic outcomes of patients with resected T3N0M0 non-small cell lung cancer. Semin Thorac Cardiovasc Surg 2023;35:796-804. doi: 10.1053/j.semtcvs.2022.08.007.
6. Cai JS, Yang F, Wang X. Reconsidering the T category for the T3 non-small cell lung cancer with additional tumor nodules in the same lobe: A population-based study. Front Oncol 2023;13:1043386. doi: 10.3389/fonc.2023.1043386.
7. Wang F, Su H, E H, Hou L, Yang M, Xu L, et al. Reconsidering T component of cancer staging for T3/T4 non-small-cell lung cancer with additional nodule. Ther Adv Med Oncol 2022;14:17588359221130502. doi: 10.1177/17588359221130502.

8. Yutaka Y, Terada K, Tanaka S, Yamada Y, Ohsumi A, Nakajima D, et al. Prognostic impact of pathologically confirmed rib invasion in patients with lung cancer requiring chest wall resection. J Thorac Dis 2022;14:4660-8. doi: 10.21037/jtd-22-976.
9. Amin MB, Greene FL, Edge SB, Compton CC, Gershenwald JE, Brookland RK, et al. The Eighth Edition AJCC Cancer Staging Manual: Continuing to build a bridge from a population-based to a more "personalized" approach to cancer staging. CA Cancer J Clin 2017;67:93-9. doi: 10.3322/caac.21388.
10. Lee CY, Byun CS, Lee JG, Kim DJ, Cho BC, Chung KY, et al. The prognostic factors of resected non-small cell lung cancer with chest wall invasion. World J Surg Oncol 2012;10:9. doi: 10.1186/1477-7819-10-9.
11. Choi Y, Lee IJ, Lee CY, Cho JH, Choi WH, Yoon HI, et al. Multi-institutional analysis of T3 subtypes and adjuvant radiotherapy effects in resected T3N0 non-small cell lung cancer patients. Radiat Oncol J 2015;33:75-82. doi: 10.3857/roj.2015.33.2.75.
12. Jeon JH, Kim MS, Moon DH, Yang HC, Hwangbo B, Kim HY, et al. Prognostic differences in subgroups of patients with surgically resected T3 non-small cell lung cancer. Ann Thorac Surg 2016;102:1630-7. doi: 10.1016/j.athoracsur.2016.04.096.
13. Wu LL, Li CW, Li K, Qiu LH, Xu SQ, Lin WK, et al. The difference and significance of parietal pleura invasion and rib invasion in pathological T classification with non-small cell lung cancer. Front Oncol 2022;12:878482. doi: 10.3389/fonc.2022.878482.
14. Komiya T, Powell E, Takamori S. Prognostic impact of single and multiple descriptors in pathologically staged T3N0M0 NSCLC. JTO Clin Res Rep 2021;2:100111. doi: 10.1016/j.jtocrr.2020.100111.
15. Cai JS, Yang F, Wang X. Is there a prognostic difference among patients with T3N0-3M0 non-small-cell lung cancer with different T3 descriptors? Eur J Cardiothorac Surg 2023;63. doi: 10.1093/ejcts/ezac558.