The European Research Journal 2025;11(2):351-362 Original Article

DOI: https://doi.org/10.18621/eurj.1633305 *Medical Oncology*

Prognostic factors and the impact of adjuvant chemotherapy on recurrence and survival in stage I non-small cell lung cancer: A real-world study

Akif Doğan[1], Sedat Yıldırım[2], Hande Nur Erölmez[3], Goncagül Akdağ[2], Zeynep Yüksel Yaşar[2], Ezgi Türkoğlu[2], Nurullah İlhan[1], Seval Ay Ersoy[2]

[1]Department of Medical Oncology, University of Health Sciences, Sancaktepe Şehit Prof. Dr. İlhan Varank Training and Research Hospital, İstanbul, Türkiye; [2]Department of Medical Oncology, University of Health Sciences, Kartal Dr. Lütfi Kırdar City Hospital, İstanbul, Türkiye; [3]Department of Family Medicine, University of Health Sciences, Sancaktepe, Şehit Prof Dr. İlhan Varank Training Research Hospital, İstanbul, Türkiye

ABSTRACT

Objectives: Non-small cell lung cancer (NSCLC) is a leading cause of cancer-related mortality. Despite curative surgery, recurrence is common in Stage I NSCLC, highlighting the need for improved prognostic classification. This study aims to evaluate the key pathological factors affecting recurrence and survival and to investigate the potential benefit of adjuvant chemotherapy (ACT) in patients with Stage I NSCLC.

Methods: A retrospective analysis was conducted on patients with Stage I NSCLC who underwent curative surgery between 2010 and 2024. Demographic and disease-related prognostic factors were assessed. The impact of these factors, along with adjuvant chemotherapy (ACT), on overall survival (OS) and disease-free survival (DFS) was analyzed.

Results: A total of 95 patients were included in the study, with a median follow-up period of 47 months. Recurrence occurred in 35.8% of patients, and 16.8% died. The five-year OS and DFS rates were calculated as 76.4% and 67.9%, respectively. Spread through air spaces (STAS) was identified as an independent prognostic factor associated with an increased risk of recurrence. While OS was shorter in patients with LVI positivity, it was not determined to be an independent prognostic factor. Visceral pleural invasion (VPI) did not demonstrate a significant prognostic impact on survival or recurrence. The effect of ACT on OS and DFS was evaluated, but no survival advantage was observed.

Conclusions: Certain pathological factors influence survival and recurrence in Stage I NSCLC. While STAS was identified as an independent prognostic factor, ACT did not provide a significant benefit for OS or DFS. These findings emphasize the importance of individualized treatment approaches and close oncological follow-up after surgery. Future studies should incorporate novel and effective biomarkers, such as circulating tumor DNA, to optimize adjuvant therapy decisions.

Keywords: Non-small cell lung cancer, spread through air spaces, recurrence, survival, prognostic factors, lymphovascular invasion, adjuvant chemotherapy

Corresponding author: Akif Doğan, MD.,
Phone: +90 216 606 33 00, E-mail: drakifd@gmail.com

How to cite this article: Doğan A, Yıldırım S, Erölmez HN, et al. Prognostic factors and the impact of adjuvant chemotherapy on recurrence and survival in stage I non-small cell lung cancer: A real-world study. Eur Res J. 2025;11(2):351-362. doi: 10.18621/eurj.1633305

Received: February 5, 2025
Accepted: February 14, 2025
Published Online: February 17, 2025

Lung cancer is the leading cause of cancer-related deaths in both men and women, posing a significant global health burden [1]. Non-small cell lung cancer (NSCLC), which accounts for approximately 85% of all lung cancer cases, is the most common subtype [1]. In patients with early-stage NSCLC, surgical treatment remains the most effective curative approach [2]. However, even after curative surgery, the risk of recurrence persists in 20-30% of patients, negatively impacting long-term survival rates [3]. The five-year survival rate for stage IB patients remains at 73%, while this rate reaches 85% in stage IA patients [3, 4]. In this context, identifying the factors influencing postoperative recurrence and survival is crucial for accurately determining which patients require adjuvant therapy. This is essential to prevent undertreatment or overtreatment, ensuring optimal management of stage I NSCLC patients.

Among the factors influencing postoperative survival, tumor size, lymphovascular invasion (LVI), visceral pleural invasion (VPI), histological subtype, and surgical margin positivity (SMP) have long been recognized. In recent years, however, spread through air spaces (STAS) has emerged as an increasingly investigated prognostic factor [5-9]. Despite numerous studies, a clear consensus has yet to be reached regarding which parameters indicate a higher recurrence risk in stage I disease, and no definitive agreement has been established on the use of adjuvant therapy. Adjuvant platinum-based chemotherapy is generally recommended for stage I NSCLC patients with tumors ≥4 cm. However, conflicting findings exist in the literature regarding the effectiveness of adjuvant chemotherapy (ACT) in patients with tumors smaller than 4 cm or those exhibiting high-risk features such as VPI or LVI [10, 11]. Current guidelines do not recommend adjuvant chemotherapy for stage 1A patients; however, they suggest chemotherapy for certain groups of patients with stage 1B disease. Specifically, adjuvant chemotherapy is recommended for patients with tumors larger than 4 cm, those showing lymphovascular invasion or pleural invasion, those with poorly differentiated tumor histology, and those with a PET scan SUV value greater than 10 [12].

This study aims to retrospectively evaluate the factors affecting recurrence and survival in NSCLC patients who underwent surgical treatment and continued oncological follow-up at a single center between 2010 and 2024. By addressing existing gaps in the literature, this study seeks to contribute to the development of improved treatment strategies for this patient population.

METHODS

Study Design and Patients

This study is a single-center cohort study that retrospectively evaluates the factors affecting prognosis in patients with stage I non-small cell lung cancer (NSCLC) who underwent surgery between 2010 and 2024. Local ethics committee approval was obtained for this study (approval number 2025/010.99/12/35), and it was conducted under the principles of the Declaration of Helsinki.

Patients included in the study were those diagnosed pathologically with stage I NSCLC who underwent lobectomy, segmentectomy, or wedge resection and at least six months of oncological follow-up after surgery. Patients with tumors containing small cell components, those who underwent inadequate lymph node dissection, those who received neoadjuvant therapy, and those with synchronous/metachronous cancer were excluded from the study. Staging was performed according to the 8th edition of the American Joint Committee on Cancer (AJCC) staging system, and histological subtypes were classified according to the World Health Organization (WHO) classification [13, 14].

Clinical Data Collection

The demographic characteristics of the patients (age, gender), tumor size, histological subtype, and pathological prognostic factors STAS, LVI, VPI, SMP, and main bronchus involvement (MBI) were retrospectively obtained from patient records.

Patients who received adjuvant chemotherapy were compared with those who did not in terms of survival and recurrence. Postoperatively, patients were followed up with computed tomography every 3 to 6 months during the first two years and then annually for at least four years. Patients who were lost to follow-up during the specified follow-up period were excluded from the analyses.

Table 1. Distribution of sociodemographic and clinical variables

Variables	Data
Age (years)	61.61±8.98 / 61.0 (37-82)
≤65 / >65	61 (64.2) / 34 (35.8)
Gender	
Female / Male	26 (27.4) / 69 (72.6)
ECOG score	
0 / 1 / 2	54 (56.8) /38 (40.0) / 3 (3.2)
Comorbidity	
Absent / Present	44 (46.3) / 51 (53.7)
Tumor location	
Right lung / Left lung	60 (63.2) / 35 (36.8)
Right lung superior / inferior lobe	34 (35.8) / 24 (25.3)
Left lung superior / inferior lobe	17 (17.9) / 20 (21.1)
Upper lobe / lower lobe	50 (56.2) / 39 (43.8)
Surgical type	
Wedge resection / lobectomy and others	16 (16.8) / 79 (83.2)
Adjuvant chemotherapy	
No / Yes	68 (71.6) / 27 (28.4)
Received adjuvant cisplatin	
Not Received / Received	6 (22.2) / 21 (77.8)
Tumor type	
Non squamous / Squamous	65 (68.4) / 30 (31.6)
MBI	
Absent / Present	91 (95.8) / 4 (4.2)
LVI	
Absent / Present	74 (77.9) / 21 (22.1)
PNI	
Absent / Present	83 (87.4) / 12 (12.6)
STAS	
Absent / Present	68 (71.6) / 27 (28.4)
Bronchial involvement	
Absent / Present	89 (93.7) / 6 (6.3)
Surgical margin	
Negative / Positive	89 (93.7) / 6 (6.3)
VPI	
Absent / Present	73 (76.8) / 22 (23.2)
Tumor stage	
T1 / T2	69 (72.6) / 26 (27.4)
TNM stage	
Stage 1A1 / 1A2 / 1A3 / 1B	13 (13.7) / 26 (27.4) / 18 (18.9) / 38 (40.0)
Recurrence	
Absent / Present	61 (64.2) / 34 (35.8)
Mortality	
Alive / Deceased	79 (83.2) / 16 (16.8)
Follow-up duration (months)	46.23±22.01 / 47.0 (8-86.0)

Data are shown as mean±standard deviation or median (minimum-maximum) or n (%) where appropriate. ECOG=Eastern Cooperative Oncology Group, MBI=Main Bronchus Involvement, LVI=Lymphovascular Invasion, PNI=Perineural Invasion, STAS=Spread Through Air Spaces, VPI=Visceral Pleural Invasion, TNM=Tumor Nod Metastasis

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 25.0 (Statistical Package for the Social Sciences, IBM Corp., Armonk, NY, USA). Descriptive statistics were presented as n and % for categorical variables and as Mean ± SD and Median (min-max) for continuous variables. The Kaplan-Meier method was used to compare survival and DFS durations between clinical groups. Finally, the results of multivariate Cox regression analysis were provided to assess the impact of various clinical variables on mortality and recurrence risk. A P-value < 0.05 was considered statistically significant.

RESULTS

The median age of the patients included in the study was 61 years (range: 37-82 years), with a male-to-female ratio of 2.8 (69/26). Wedge resection was performed in 16 patients (16.8%), while the remaining patients underwent anatomical resection (lobectomy, pneumonectomy, etc.). The most common tumor location was the right upper lobe (n=34, 35.8%). Histologically, 30 patients (31.6%) had squamous cell carcinoma, while 65 patients (68.4%) had non-squamous histology. A total of 27 patients (28.4%) received ACT, of whom 21 (77.8%) were treated with a cis-

Table 2. Overall survival (OS) comparisons

Variables	2 years (%)	5 years (%)	Median (95% CI)	P value
General	93.6	80.4	- (-)	
Age				
≤65	93.3	81.9	- (-)	0.976
>65	94.1	76.8	- (-)	
Gender				
Female	96.2	96.2	- (-)	0.051
Male	92.6	74.2	- (-)	
ECOG score				
0	94.2	84.6	- (-)	0.718
1	94.7	75.8	- (-)	
2	66.7	66.7	- (-)	
Comorbidity				
Absent	90.8	70.7	- (-)	0.109
Present	96.1	87.8	- (-)	
Tumor location				
Right lung superior lobe	97.1	88.8	- (-)	0.796
Right lung inferior lobe	95.8	69.7	- (-)	
Left lung superior lobe	81.9	73.7	- (-)	
Left lung inferior lobe	95.0	80.9	- (-)	
Right lung	95.0	81.5	- (-)	0.945
Left lung	91.0	78.5	- (-)	
Upper lobe	93.8	85.5	- (-)	0.519
Lower lobe	94.9	70.9	- (-)	
Surgical type				
Wedge resection	100.0	85,7	- (-)	0.267
Lobectomy and others	92.3	79,3	- (-)	
Adjuvant chemotherapy				
Absent	95.5	80.0	- (-)	0.927
Present	88.9	82.1	- (-)	

Table 2 contunied. Overall survival (OS) comparisons

Variables	2 years (%)	5 years (%)	Median (95% CI)	P value
Adjuvant cisplatin				
Absent	83.3	83.3	- (-)	0.850
Present	90.5	81.4	- (-)	
Tumor type				
Non squamous	93.7	80.4	- (-)	0.731
Squamous	93.3	80.2	- (-)	
MBI				
Absent	94.4	80.6	- (-)	0.526
Present	75.0	75.0	- (-)	
LVI				
Absent	94.4	84.8	- (-)	**0.030**
Present	90.5	68.4	79.00 (51.21-106.78)	
PNI				
Absent	93.8	81.6	- (-)	0.665
Present	91.7	73.3	- (-)	
STAS				
Absent	94.0	84.3	- (-)	0.053
Present	92.6	71.3	79.00 (60.20-97.79)	
Bronchial involvement				
Absent	94.3	81.2	- (-)	0.442
Present	83.3	66.7	- (-)	
Surgical margin				
Negative	95.4	83.4	- (-)	**0.002**
Positive	66.7	33.3	48.00 (0.00-106.38)	
VPI				
Absent	93.0	76.6	- (-)	0.329
Present	95.5	95.5	- (-)	
Tumor stage				
T1	94.1	77.4	- (-)	0.703
T2	92.3	87.2	- (-)	
TNM stage				
Stage 1A1	91.7	73.3	- (-)	0.343
Stage 1A2	96.2	84.6	- (-)	
Stage 1A3	94.4	65.4	79.00 (-)	
Stage 1B	92.1	87.9	- (-)	

ECOG=Eastern Cooperative Oncology Group, MBI=Main Bronchus Involvement, LVI=Lymphovascular Invasion, PNI=Perineural Invasion, STAS=Spread Through Air Spaces, VPI=Visceral Pleural Invasion, TNM=Tumor Nod Metastasis Kaplan-Meier, Log-rank test, P<0.05 statistically significant

platin-containing regimen. The median follow-up period was 47 months (range: 8-86 months). During this period, recurrence was observed in 34 patients (35.8%), and 16 patients (16.8%) died. The pathological characteristics of the patients and treatment approaches are summarized in Table 1.

The median overall survival (OS) and disease-free survival (DFS) were not reached. The two-year and

five-year OS rates were calculated as 93.6% and 80.4%, respectively, while the two-year and five-year DFS rates were 77.4% and 56%, respectively. Comparisons of OS and DFS according to different variables are presented in Tables 2 and 3, respectively.

For patients with negative LVI, the median OS was not reached, whereas for those with positive LVI, the median OS was 79 months, showing a statistically significant difference (P=0.03) (Fig. 1). Similarly, in patients with negative surgical margins, the median OS was not reached, while in those with positive margins, the median OS was 48 months, with a statistically significant difference (P=0.002). There was no statistically significant difference in OS between patients with and without VPI (P=0.329) (Fig. 1). Univariate analysis identified variables significantly associated with OS, which were subsequently included in a multivariate Cox regression model. According to this analysis, SMP were found to increase the risk of death by 4.83 times (HR: 4.83, 95% CI: 1.33-17.51, P=0.016).

In univariate analysis, MBI (P=0.011), STAS (P=0.008), and SMP (P=0.009) were found to be statistically significant for DFS (Table 3). The median DFS was not reached in patients without STAS, whereas in those with STAS, the median DFS was 42 months, showing a statistically significant difference (P=0.008) (Fig. 2). Similarly, the median DFS was not reached in patients with negative surgical margins, while it was 33 months in those with positive margins, with a statistically significant difference (P=0.009). Variables found to be significant for DFS in univariate analysis were included in the multivariate Cox regression model. According to the model results, MBI increased the risk of recurrence by 4.46 times (HR: 4.46, 95% CI: 1.26-15.69, P=0.020), the presence of STAS

Table 3. Disease-free survival (DFS) comparisons

Variables	2 years (%)	5 years (%)	Median (95% CI)	P value
General	77.4	56.0	- (-)	
Age				
≤65	77.7	61.4	- (-)	0.470
>65	76.5	45.9	53.00 (-)	
Gender				
Female	88.1	68.8	- (-)	0.081
Male	73.4	50.9	- (-)	
ECOG score				
0	78.7	53.2	- (-)	0.407
1	76.2	61.1	- (-)	
2	66.7	-	30.00 (0.0-65.20)	
Comorbidity				
Absent	74.5	53.6	- (-)	0.667
Present	79.7	58.0	- (-)	
Tumor location				
Right lung superior lobe	76.2	55.2	- (-)	0.891
Right lung inferior lobe	78.6	45.0	48.00 (-)	
Left lung superior lobe	81.6	64.9	- (-)	
Left lung inferior lobe	74.7	59.4	- (-)	
Right lung	76.2	49.7	53.00 (-)	0.291
Left lung	79.5	66.6	- (-)	
Upper lobe	79.7	59.7	- (-)	0.588
Lower lobe	76.2	53.9	- (-)	

Table 3 contunied. **Disease-free survival (DFS) comparisons**

Variables	2 years (%)	5 years (%)	Median (95% CI)	P value
Surgical type				
Wedge resection	81.3	67.7	- (-)	0.465
Lobectomy and others	76.5	53.7	- (-)	
Adjuvant chemotherapy				
Absent	82.2	56.7	- (-)	0.089
Present	64.6	47.9	34.00 (-)	
Adjuvant cisplatin				
Absent	50.0	33.3	12.00 (0.00-39.60)	0.251
Present	68.2	51.9	- (-)	
Tumor type				
Non squamous	81.0	63.7	- (-)	0.064
Squamous	70.0	42.6	48.00 (25.53-70.46)	
MBI				
Absent	79.7	57.1	- (-)	0.011
Present	25.0	25.0	5.00 (-)	
LVI				
Absent	83.3	59.4	- (-)	0.064
Present	57.1	44.4	48.00 (3.45-92.54)	
PNI				
Absent	76.4	56.8	- (-)	0.970
Present	83.3	54.0	- (-)	
STAS				
Absent	83.2	65.0	- (-)	0.008
Present	62.7	33.6	42.00 (22.79-61.20)	
Bronchial involvement				
Absent	79.3	57.5	- (-)	0.091
Present	50.0	33.3	20.00 (0.00-52.40)	
Surgical margin				
Negative	78.3	59.1	- (-)	0.009
Positive	66.7	-	33.00 (0.00-74.91)	
VPI				
Absent	76.4	58.1	- (-)	0.860
Present	80.2	43.8	53.00 (27.63-78.36)	
Tumor stage				
T1	82.2	61.2	- (-)	0.111
T2	64.8	41.6	52.00 (22.51-81.48)	
TNM stage				
Stage 1A1	61.5	52.7	- (-)	0.331
Stage 1A2	92.3	70.3	- (-)	
Stage 1A3	82.6	47.2	50.00 (-)	
Stage 1B	70.1	48.4	53.00 (-)	

ECOG=Eastern Cooperative Oncology Group, MBI=Main Bronchus Involvement, LVI=Lymphovascular Invasion, PNI=Perineural Invasion, STAS=Spread Through Air Spaces, VPI=Visceral Pleural Invasion, TNM=Tumor Nod Metastasis Kaplan-Meier, Log-rank test, P<0.05 statistically significant

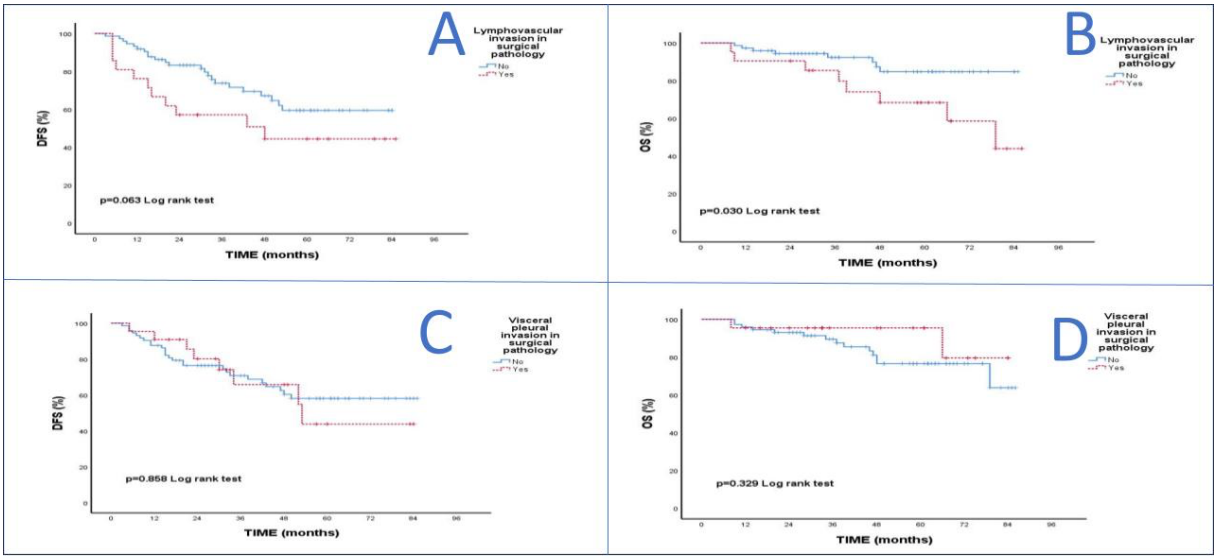

Fig. 1. Kaplan-Meier estimates for disease-free (A) and overall (B) survival, by lymphovascular invasion. Disease-free (C) and overall (D) survival, by visceral pleural invasion.

increased the recurrence risk by 2.79 times (HR: 2.79, 95% CI: 1.39-5.60, P=0.004), and SMP increased the recurrence risk by 4.35 times (HR: 4.35, 95% CI: 1.43-13.24, P=0.019).

In both patients who received and did not receive ACT, the median OS was not reached. The two-year OS rate was 95.5% in patients who did not receive ACT and 88.9% in those who did (Fig. 3). The five-year OS rate was 80% in patients without ACT and 82% in those with ACT, with no statistically significant difference (P=0.927). Regarding DFS, the median DFS was 34 months in patients who received ACT, whereas it was not reached in those who did not receive it. The two-year DFS rate was 82.2% in patients without ACT and 64.6% in those with ACT. The five-year DFS rate was 56.7% in patients without ACT and

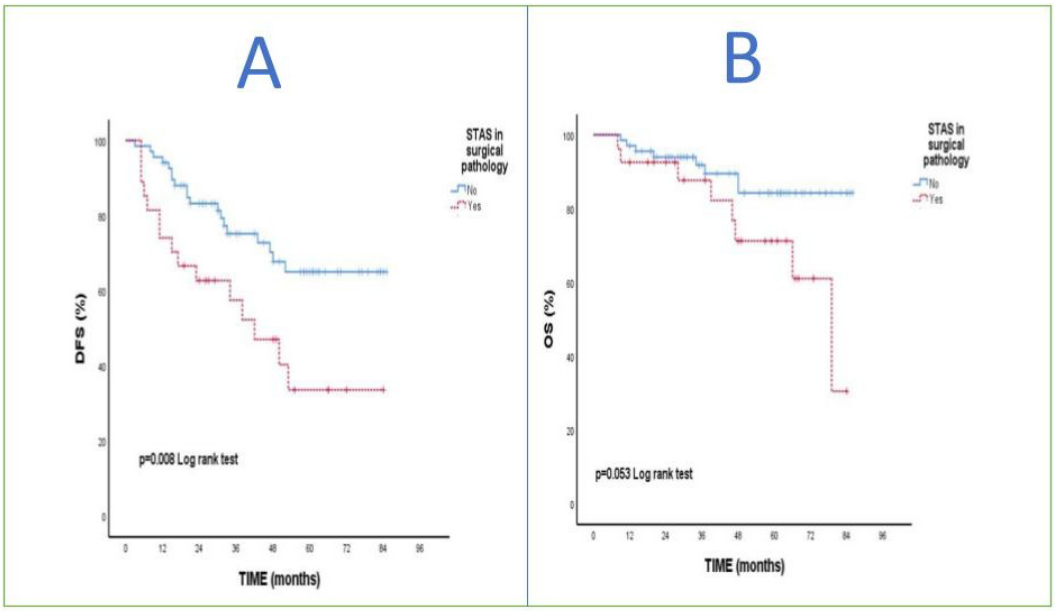

Fig. 2. Kaplan-Meier estimates for disease-free (A) and overall (B) survival, by STAS.

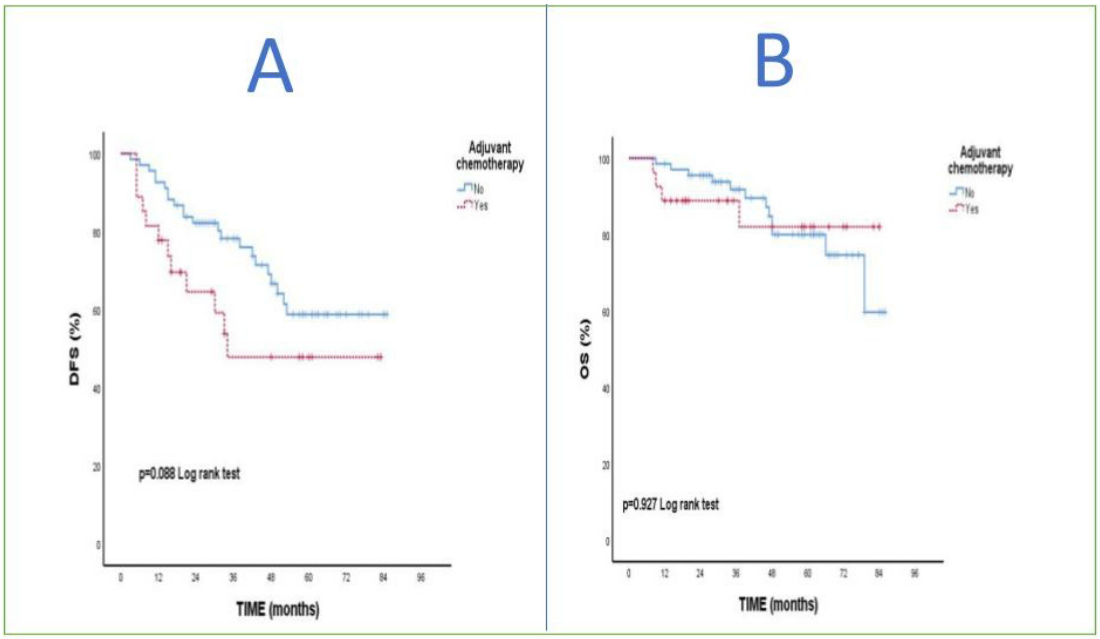

Fig. 3. Kaplan-Meier estimates for disease-free (A) and overall (B) survival, by adjuvant chemotherapy.

47.9% in those with ACT, with no statistically significant difference (P=0.089) (Fig. 3).

To assess the impact of adjuvant chemotherapy in high-risk patients a subgroup analysis was conducted. Among patients over 65 years old who did not receive adjuvant chemotherapy had a significantly longer DFS (P<0.05). However, in subgroup analyses based on other high-risk factors, no statistically significant difference was found in OS or DFS between patients who received adjuvant chemotherapy and those who did not (Fig. 4).

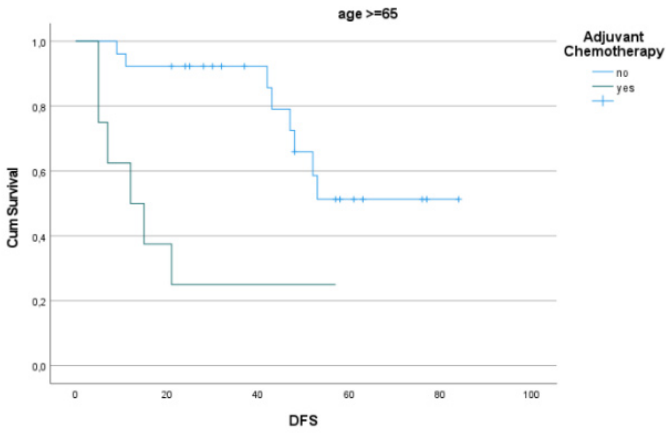

Fig. 4. Effects of adjuvant chemotherapy on disease-free survival in patients over 65 years old.

DISCUSSION

The identification of poor prognostic factors in stage I NSCLC patients is of great importance for predicting the course of the disease after surgery and optimizing adjuvant treatment strategies. However, no standardized consensus has been reached in the literature, and different variables are highlighted in various studies. In our study, while SCP, MBI, and STAS were found to be significant determinants of survival and recurrence, factors such as age, gender, histological subtype, ACT, LVI, and VPI - considered prognostically important in the literature - were not identified. It is well known that prognostic factors in stage I NSCLC are not consistently determined across studies and may vary between different patient populations. Our findings reflect this heterogeneity, emphasizing the need for standardization of prognostic markers in stage I disease and a more individualized, patient-centered approach.

STAS, which defines tumor spread through air spaces, is a histopathological feature increasingly recognized for its prognostic significance and is associated with poor prognosis in early-stage NSCLC [15]. While various studies have shown that anatomical resection may not be necessary for every stage I NSCLC

patient, it has been reported that wider surgical resections, such as lobectomy, provide better survival outcomes, particularly in STAS-positive patients [16]. Our study detected STAS positivity in 2 of the 16 patients who underwent wedge resection, and both experienced recurrences. In contrast, among the 14 STAS-negative patients, recurrence was observed in only 2 cases. Although further analysis could not be performed due to the small sample size, this finding supports the notion that wedge resection may be an inadequate surgical option for STAS-positive patients and that lobectomy may be a more appropriate approach [16, 17].

VPI is a crucial pathological finding indicating tumor extension to the pleural surface and, in the current TNM staging system, leads to an upgrade to T2 classification regardless of tumor size. This underscores the prognostic significance of VPI; however, some studies suggest that in smaller tumors, LVI may be a stronger prognostic factor than VPI [7]. In our study, LVI was found to be significant in univariate survival analysis, but its borderline significance in multivariate analysis suggests that this may be due to the small cohort size. The lack of a significant effect of VPI on survival or recurrence aligns with the literature suggesting that LVI may be biologically more aggressive than VPI in smaller tumors. Given that most of our patient population had tumors ≤3 cm, this could explain why VPI did not appear to have a significant impact [7, 18]. However, large-scale studies are needed to make a definitive conclusion on this matter.

Studies on prognostic factors in stage I NSCLC indicate that while some factors have well-established prognostic significance, others show variability. SMP and MBI have been identified in numerous studies as poor prognostic factors for survival and recurrence [16, 19, 20], and our study confirmed them as independent prognostic indicators. Conversely, factors such as age, male gender, and histological subtype have shown inconsistent prognostic value in the literature, and our study did not find a significant association between these variables and survival or recurrence [3, 21, 22]. This discrepancy may be due to differences in patient populations, treatment approaches, or the limited sample size. To improve prognostic accuracy in stage I NSCLC, larger-scale studies and the use of biomarkers are necessary.

The efficacy of ACT in stage I NSCLC remains controversial, and proper identification of high-risk patients is essential. The LACE meta-analysis demonstrated that adjuvant chemotherapy provides a survival benefit for tumors larger than 4 cm but does not significantly contribute to smaller tumors [10]. Various studies have reported that adjuvant therapy improves survival in tumors >3 cm or those with positive VPI [23-25]. In our study, no significant survival difference was observed between patients who received ACT and those who did not, which may be attributed to the limited sample size and treatment selection heterogeneity.

In addition to conventional prognostic factors, recent research has investigated the prognostic and predictive value of biomarkers such as circulating tumor DNA (ctDNA). The literature suggests that preoperative ctDNA presence is associated with a high risk of recurrence in early-stage NSCLC patients and that these patients may derive greater benefit from adjuvant chemotherapy [26]. When considered alongside high-risk factors such as STAS and SMP, ctDNA is believed to be a valuable tool for guiding adjuvant therapy decisions. Although ctDNA was not assessed in our study, incorporating ctDNA into future research alongside standard prognostic factors may contribute to a more accurate determination of the need for adjuvant therapy in stage I NSCLC.

Our study confirms that STAS, LVI, SMP, and MBI are poor prognostic factors in stage I NSCLC, whereas VPI, age, gender, and histological subtype were not found to be significant. In subgroup analyses of adjuvant chemotherapy, it was concluded that adjuvant chemotherapy showed detrimental impact on DFS in patients aged over 65 and was ineffective in patients with other risk factors. However, these findings may be due to the small sample size and patient heterogeneity. The impact of adjuvant chemotherapy on survival remains unclear, necessitating better identification of high-risk patients. In the future, integrating biomarkers such as ctDNA with pathological factors like STAS and LVI may improve patient selection. Larger-scale studies are needed to establish personalized treatment approaches for stage I NSCLC.

Limitations

This study has some limitations. Its single-center retrospective design may limit generalizability, and the small sample size in certain subgroups may reduce statistical power, making it difficult to draw definitive

conclusions about the impact of adjuvant chemotherapy. Additionally, the absence of molecular biomarker analyses, such as ctDNA, restricts the ability to fully stratify high-risk patients. Another important limitation is the long study period, during which changes in staging systems and evolving chemotherapy indications may have influenced treatment decisions. This variability could have introduced heterogeneity into the study population, affecting the consistency of the results. However, a strength of this study is the inclusion of relatively novel prognostic factors, such as STAS. Future multicenter prospective studies incorporating molecular profiling may help refine risk stratification and optimize treatment strategies.

CONCLUSION

In this retrospective study, we identified key prognostic factors influencing recurrence and survival in stage I NSCLC patients who underwent surgical treatment. Our findings demonstrate that STAS, LVI, SMP, and MBI are significant predictors of poor outcomes, whereas VPI, age, sex, and histological subtype did not show a statistically significant impact on survival or recurrence. The role of ACT in stage I NSCLC remains inconclusive, as our analysis did not confirm a definitive survival benefit. However, our findings emphasize the importance of risk stratification to avoid both overtreatment and undertreatment in this patient population. Given the heterogeneity of prognostic factors, individualized treatment approaches remain crucial in optimizing outcomes. Emerging biomarkers such as ctDNA may offer additional insights into recurrence risk and could refine patient selection for adjuvant therapy. Future large-scale prospective studies incorporating molecular profiling and pathological markers such as STAS and LVI are needed to establish more precise prognostic models and personalized treatment strategies for stage I NSCLC. Our study contributes to the growing body of literature advocating for a standardized risk assessment model to guide treatment decisions in stage I NSCLC. By integrating both histopathological and molecular prognostic factors, we can improve risk-adapted therapy and enhance long-term survival in surgically treated NSCLC patients.

Ethical Statement

This study was approved by the Kartal Dr. Lütfi Kırdar City Hospital Scientific Research Ethics Committee (Decision no: 2025/010.99/12/35 and date:24.01.2025) and was conducted in accordance with the principles of the Declaration of Helsinki.

Authors' Contribution

Study Conception: AD; Study Design: AD, SY, HNE; Supervision: GA, ZYY; Funding: AD, Nİ; Materials: AD, Nİ; Data Collection and/or Processing: AD, ZYY, ET; Statistical Analysis and/or Data Interpretation: AD, GA, ET; Literature Review: AD, HNE; Manuscript Preparation: AD, HNE; and Critical Review: SY, HNE, SAE.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

Financing

The authors disclosed that they did not receive any grant during conduction or writing of this study.

REFERENCES

1. Siegel RL, Kratzer TB, Giaquinto AN, Sung H, Jemal A. Cancer statistics, 2025. CA Cancer J Clin. 2025;75(1):10-45. doi: 10.3322/caac.21871.
2. Stirling RG, Chau C, Shareh A, Zalcberg J, Fischer BM. Effect of Follow-Up Surveillance After Curative-Intent Treatment of NSCLC on Detection of New and Recurrent Disease, Retreatment, and Survival: A Systematic Review and Meta-Analysis. J Thorac Oncol. 2021;16(5):784-797. doi: 10.1016/j.jtho.2021.01.1622.
3. Choi PJ, Jeong SS, Yoon SS. Prognosis of recurrence after complete resection in early-stage non-small cell lung cancer. Korean J Thorac Cardiovasc Surg. 2013;46(6):449-56. doi: 10.5090/kjtcs.2013.46.6.449.
4. Dediu M, Ion O, Ion R, et al. Impact of adjuvant chemotherapy in stage IB non-small-cell lung cancer: an analysis of 112 consecutively treated patients. J BUON. 2012;17(2):317-322.
5. Mollberg NM, Bennette C, Howell E, Backhus L, Devine B, Ferguson MK. Lymphovascular invasion as a prognostic indicator in stage I non-small cell lung cancer: a systematic review and meta-analysis. Ann Thorac Surg. 2014;97(3):965-971. doi: 10.1016/j.athoracsur.2013.11.002.
6. Oven Ustaalioglu BB, Unal OU, Turan N, et al. Prognostic factors for lymph node negative stage I and IIA non-small cell lung cancer: multicenter experiences. Asian Pac J Cancer Prev. 2013;14(11):6287-6292. doi: 10.7314/apjcp.2013.14.11.6287.

7. Tao H, Hayashi T, Sano F, et al. Prognostic impact of lymphovascular invasion compared with that of visceral pleural invasion in patients with pN0 non-small-cell lung cancer and a tumor diameter of 2 cm or smaller. J Surg Res. 2013;185(1):250-254. doi: 10.1016/j.jss.2013.05.104.
8. Neri S, Yoshida J, Ishii G, et al. Prognostic impact of microscopic vessel invasion and visceral pleural invasion in non-small cell lung cancer: a retrospective analysis of 2657 patients. Ann Surg. 2014;260(2):383-388. doi: 10.1097/sla.0000000000000617.
9. Ding Y, Li J, Li X, Xu M, Geng H, Sun D. Impact of preoperative biopsy on tumor spread through air spaces in stage I non-small cell lung cancer: a propensity score-matched study. BMC Pulm Med. 2022;22(1):293. doi: 10.1186/s12890-022-02090-z.
10. Pignon JP, Tribodet H, Scagliotti GV, et al. Lung adjuvant cisplatin evaluation: a pooled analysis by the LACE Collaborative Group. J Clin Oncol. 2008;26(21):3552-3559. doi: 10.1200/jco.2007.13.9030.
11. Strauss GM, Herndon JE, 2nd, Maddaus MA, et al. Adjuvant paclitaxel plus carboplatin compared with observation in stage IB non-small-cell lung cancer: CALGB 9633 with the Cancer and Leukemia Group B, Radiation Therapy Oncology Group, and North Central Cancer Treatment Group Study Groups. J Clin Oncol. 2008;26(31):5043-5051. doi: 10.1200/jco.2008.16.4855.
12. Riely GJ, Wood DE, Ettinger DS, et al. Non-Small Cell Lung Cancer, Version 4.2024, NCCN Clinical Practice Guidelines in Oncology. J Natl Compr Canc Netw. 2024;22(4):249-274. doi: 10.6004/jnccn.2204.0023.
13. Goldstraw P, Chansky K, Crowley J, et al. The IASLC Lung Cancer Staging Project: Proposals for Revision of the TNM Stage Groupings in the Forthcoming (Eighth) Edition of the TNM Classification for Lung Cancer. J Thorac Oncol. 2016;11(1):39-51. doi: 10.1016/j.jtho.2015.09.009.
14. Travis WD. The 2015 WHO classification of lung tumors. Pathologe. 2014;35 Suppl 2:188. doi: 10.1007/s00292-014-1974-3.
15. Chen D, Mao Y, Wen J, et al. Tumor Spread Through Air Spaces in Non-Small Cell Lung Cancer: A Systematic Review and Meta-Analysis. Ann Thorac Surg. 2019;108(3):945-954. doi: 10.1016/j.athoracsur.2019.02.045.
16. Hashinokuchi A, Akamine T, Toyokawa G, et al. Impact of the distance of spread through air spaces in non-small cell lung cancer. Interdiscip Cardiovasc Thorac Surg. 2024;40(1):ivae181. doi: 10.1093/icvts/ivae181.
17. Li J, Wang Y, Li J, Cao S, Che G. Meta-analysis of Lobectomy and Sublobar Resection for Stage I Non-small Cell Lung Cancer With Spread Through Air Spaces. Clin Lung Cancer. 2022;23(3):208-213. doi: 10.1016/j.cllc.2021.10.004.
18. Lin X, Xu H, Chen J, Wu J, Lin J, Wu H. The prognosis and treatment consideration for non-small cell lung carcinoma patients with tumor size of >2.0-3.0 cm and visceral pleural invasion: a SEER-based study. Transl Cancer Res. 2024;13(11):6004-6017. doi: 10.21037/tcr-24-33.
19. Wang G, Ye YQ, Xie BL, Lai XM, Zhong SP. Investigation of the non-small cell lung cancer patients with bronchus involvements: A population-based study. Clin Respir J. 2023;17(9):941-950. doi: 10.1111/crj.13683.
20. Nagano M, Sato M. Impact of surgical margin after sublobar resection of lung cancer: a narrative review. J Thorac Dis. 2023;15(10):5750-5759. doi: 10.21037/jtd-23-711.
21. Sawabata N, Miyaoka E, Asamura H, et al. Japanese lung cancer registry study of 11,663 surgical cases in 2004: demographic and prognosis changes over decade. J Thorac Oncol. 2011;6(7):1229-1235. doi: 10.1097/JTO.0b013e318219aae2.
22. Tantraworasin A, Saeteng S, Lertprasertsuke N, Arayawudhikule N, Kasemsarn C, Patumanond J. Completely resected n0 non-small cell lung cancer: prognostic factors affecting long-term survival. ISRN Surg. 2013;2013:175304. doi: 10.1155/2013/175304.
23. Kato H, Ichinose Y, Ohta M, et al. A randomized trial of adjuvant chemotherapy with uracil-tegafur for adenocarcinoma of the lung. N Engl J Med. 2004;350(17):1713-1721. doi: 10.1056/NEJMoa032792.
24. Hamada C, Tanaka F, Ohta M, et al. Meta-analysis of postoperative adjuvant chemotherapy with tegafur-uracil in non-small-cell lung cancer. J Clin Oncol. 2005;23(22):4999-5006. doi: 10.1200/jco.2005.09.017.
25. Ak N, Ozkan B, Yenigun MB, et al. The role of adjuvant chemotherapy in resected stage I non - small cell lung cancer: A Turkish Oncology Group Study. J BUON. 2021;26(3):819-29.
26. Lu J, Feng Y, Guo K, Sun L, Ruan S, Zhang K. Prognostic value of preoperative circulating tumor DNA in non-small cell lung cancer: a systematic review and meta-analysis. J Cancer Res Clin Oncol. 2024;150(1):25. doi: 10.1007/s00432-023-05550-z.