Original Article

Access this article online
Quick Response Code:

Website:
https://eurasianjpulmonol.org
DOI:
10.14744/ejp.2025.08435

Prognostic factors affecting survival in surgically treated non-small cell lung cancer patients with chest wall invasion: A retrospective single-center study

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Abstract:

BACKGROUND AND AIM: Chest wall invasion in non-small cell lung cancer (NSCLC) was once considered a criterion for inoperability. However, with advances in thoracic surgery, complete resection in selected patients has been associated with improved outcomes. This study aims to evaluate prognostic factors influencing survival in surgically treated NSCLC patients with chest wall invasion.

METHODS: We retrospectively reviewed 77 patients who underwent pulmonary resection with chest wall resection or extrapleural resection for NSCLC with confirmed chest wall invasion between January 2000 and April 2005. Clinicopathological data, including tumor histology, tumor-node-metastasis (TNM) staging, depth of chest wall invasion, perineural and lymphatic invasion, necrosis, and surgical margin status, were analyzed. Survival was assessed using Kaplan-Meier analysis, and multivariate analysis was performed using Cox regression.

RESULTS: The five-year survival rate was 29%, with a median survival of 19 months. Complete resection (R0) was achieved in 71.7% of patients. Univariate analysis showed that positive margins, lymphatic invasion, and N2 status were associated with worse outcomes but did not reach statistical significance. In multivariate analysis, R1 resection was identified as an independent negative prognostic factor (hazard ratio: 1.96; 95% confidence interval: 1.03-3.71; p=0.04). Costal invasion appeared to be associated with better survival, though this was not statistically significant.

CONCLUSIONS: Complete surgical resection is a key determinant of survival in NSCLC with chest wall involvement. Margin status remains the most critical prognostic factor, underscoring the importance of radical oncologic surgery.

Keywords:

Chest wall invasion, non-small cell lung cancer, survival, thoracic surgery

This article is produced from a thesis.

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Received: 10-06-2025
Revised: 31-07-2025
Accepted: 01-08-2025
Published: 30-10-2025

How to cite this article: Fazlıoğlu M, Fazlıoğlu N, Bedirhan MA. Prognostic factors affecting survival in surgically treated non-small cell lung cancer patients with chest wall invasion: A retrospective single-center study. Eurasian J Pulmonol 2025;27:159-165.

Introduction

Lung cancer remains the leading cause of cancer-related deaths worldwide, with non-small cell lung cancer (NSCLC) accounting for the majority of cases. Surgical resection is the mainstay of treatment for early-stage NSCLC, yet only a limited proportion of patients are diagnosed at a stage suitable for surgery. Among surgically treated NSCLC patients, chest wall invasion is observed in approximately 5–8% of cases.[1,2]

Historically, chest wall invasion was considered a contraindication to surgery. However, since Coleman's pivotal study in 1947, it has been shown that en bloc resection of the lung and chest wall may yield acceptable survival outcomes in selected patients.[3] Complete resection with negative margins (R0) has since become a key objective in such cases.[4]

Although tumor-node-metastasis (TNM) staging remains the cornerstone of treatment planning and prognostication in NSCLC,[5] recent studies have highlighted the additional prognostic value of histopathologic features such as lymphovascular invasion,[6] perineural invasion,[7] tumor necrosis,[8] and the extent of chest wall involvement.[9,10] Nonetheless, the prognostic significance of these factors remains controversial, particularly in small retrospective series.[11,12]

This study aimed to assess the impact of various clinicopathological and surgical parameters on overall survival in NSCLC patients who underwent surgical resection with confirmed chest wall invasion.

Materials and Methods

A retrospective analysis was conducted on 77 patients with pathologically confirmed NSCLC and chest wall invasion who underwent surgery between January 2000 and April 2005 at a single tertiary hospital.

All patients were evaluated preoperatively with clinical examination, laboratory tests, pulmonary function tests, chest radiography, and thoracic computed tomography. Where indicated, ventilation-perfusion scans, brain computed tomography (CT), abdominal ultrasound, and bone scintigraphy were also performed. Mediastinal staging was carried out using CT and mediastinoscopy.

Surgical procedures included posterolateral thoracotomy, pulmonary resection, and either extrapleural or en bloc chest wall resection, depending on intraoperative Patients with tumors firmly adherent to the chest wall and exhibited macroscopic invasion beyond the parietal pleura underwent en bloc chest wall resection, including resection of adjacent ribs and intercostal tissues. In contrast, when the tumor could be easily mobilized from the chest wall and invasion was presumed to be limited to the parietal pleura, extrapleural resection was performed. Systematic lymph node sampling was performed in all cases. Frozen-section analysis guided decisions regarding resectability.

Histopathologic features analyzed from surgical specimens included histologic subtype, tumor necrosis, lymphatic and perineural invasion, and resection margin status. Although patients were originally staged according to the 1997 American Joint Committee on Cancer (AJCC) TNM classification, restaging based on the 8th edition was applied where data allowed, to enhance the comparability and relevance of prognostic evaluation.

Survival data were collected through direct follow-up and telephone contact. The survival period was calculated from the date of surgery. Kaplan-Meier survival analysis and the log-rank test were used for univariate analysis, and the Cox proportional hazards model was used for multivariate analysis. A p-value <0.05 was considered statistically significant.

The study was conducted in accordance with the 1964 Declaration of Helsinki. Artificial intelligence (AI) technology was not used in the preparation of this article. Due to the retrospective design of the study, patient consent was not obtained.

Results

A total of 77 patients with NSCLC and chest wall invasion were included in the study, with a male predominance (97.4%) and a mean age of 57±10.8 years. Right-sided tumors accounted for 64% of cases. Chest wall resection was performed in 56 patients (73%), while extrapleural resection was performed in 21 patients (27%) (Table 1).

Histopathologically, 45.4% had squamous cell carcinoma, 41.5% had adenocarcinoma, and the remainder

Table 1: Patient characteristics

Parameter	n	%
Sex		
Male	75	97.4
Female	2	2.6
Mean age (years)	57±10.8	
Side		
Right lung tumors	50	64
Left lung tumors	27	36
Resection type		
En bloc resection	56	73
Extrapleural resection	21	27
Histology		
Squamous cell carcinoma	35	45.4
Adenocarcinoma	32	41.5
Large cell carcinoma	6	7.7
Undifferentiated	1	1.2
Others	3	3.8
Stage		
IIB (T3N0M0)	38	49.4
IIIA (T3N1M0)	35	45.4
IIIA (T3N2M0)	4	5.2
Resection completeness		
Complete resection (R0)	55	71.7
Incomplete resection (R1)	21	28.3
Necrosis		
Present	66	85.7
Absent	11	14.3
Lymphatic invasion		
Present	65	84.4
Absent	12	15.6
Pleural invasion		
Present	18	23.3
Absent	59	76.6

had other subtypes. Pathological staging revealed 49.4% in stage IIB, 45.4% in stage IIIA (T3N1M0), and 5.2% in stage IIIA (T3N2M0).

Complete (R0) resection was achieved in 55 patients (71.7%). Perineural invasion was observed in 23.3%, lymphatic invasion in 84.4%, and tumor necrosis in 85.7% of cases. The five-year cumulative survival rate was 29%, and the median overall survival was 19 months (95% confidence interval [CI]: 14–24) [Fig. 1]. Patients with R0 resection had better survival compared with those with R1 margins (HR: 2.10; 95% CI: 1.12–3.91; p=0.12) in univariate analysis, although this difference was not statistically significant. In multivariate analysis, R1 resection emerged as an independent predictor of poorer survival (HR: 1.96; 95% CI: 1.03–3.71; p=0.04) (HR: 1.96, 95% CI: 1.03–3.71; p=0.04) [Figs. 1-3] (Table 2).

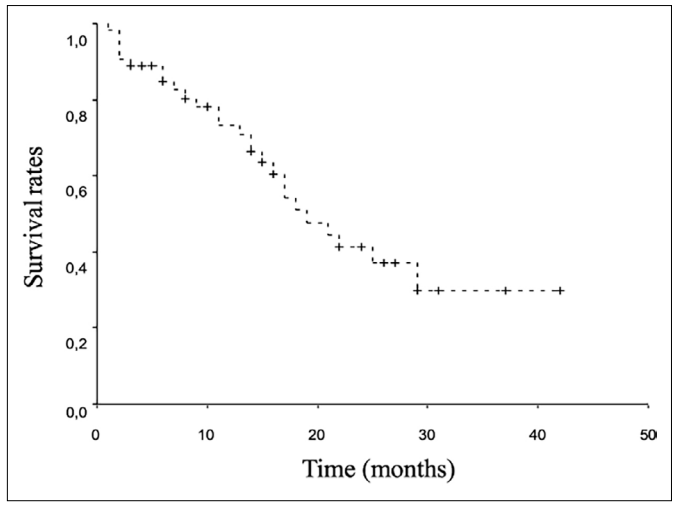

Figure 1: Kaplan-Meier overall survival curve for all patients with non-small cell lung cancer and chest wall invasion who underwent surgical resection. The five-year cumulative survival rate was 29%, with a median overall survival of 19 months

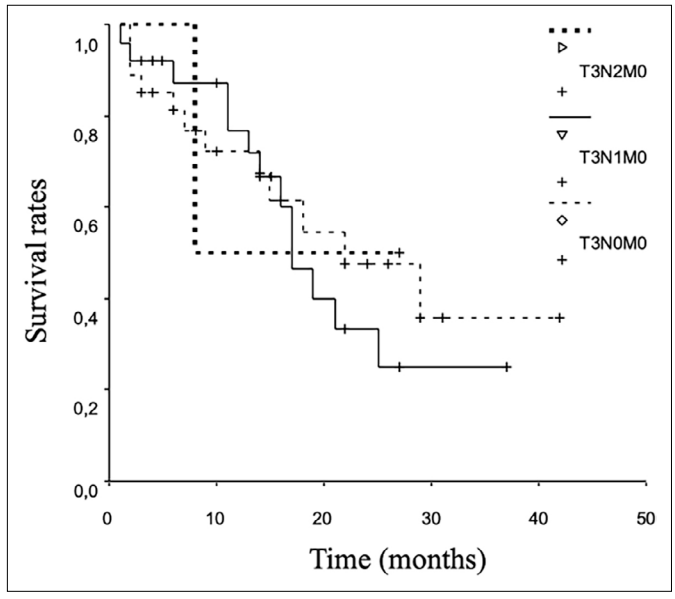

Figure 2: Kaplan-Meier survival curves according to clinical stage (T3N0M0, T3N1M0, and T3N2M0). Although the differences were not statistically significant, a trend toward decreased survival was observed with increasing nodal involvement

Subgroup analysis showed no statistically significant differences in survival based on histologic subtype (p=0.71), perineural invasion (p=0.65), lymphatic invasion (p=0.18), or tumor necrosis (p=0.27). Similarly, age did not reach statistical significance as a continuous variable (p=0.14).

Regarding the extent of chest wall invasion, no significant survival difference was observed between patients with costal involvement and those with parietal pleura invasion (HR: 0.81, 95% CI: 0.45–1.45; p=0.11), though costal involvement was associated with slightly better

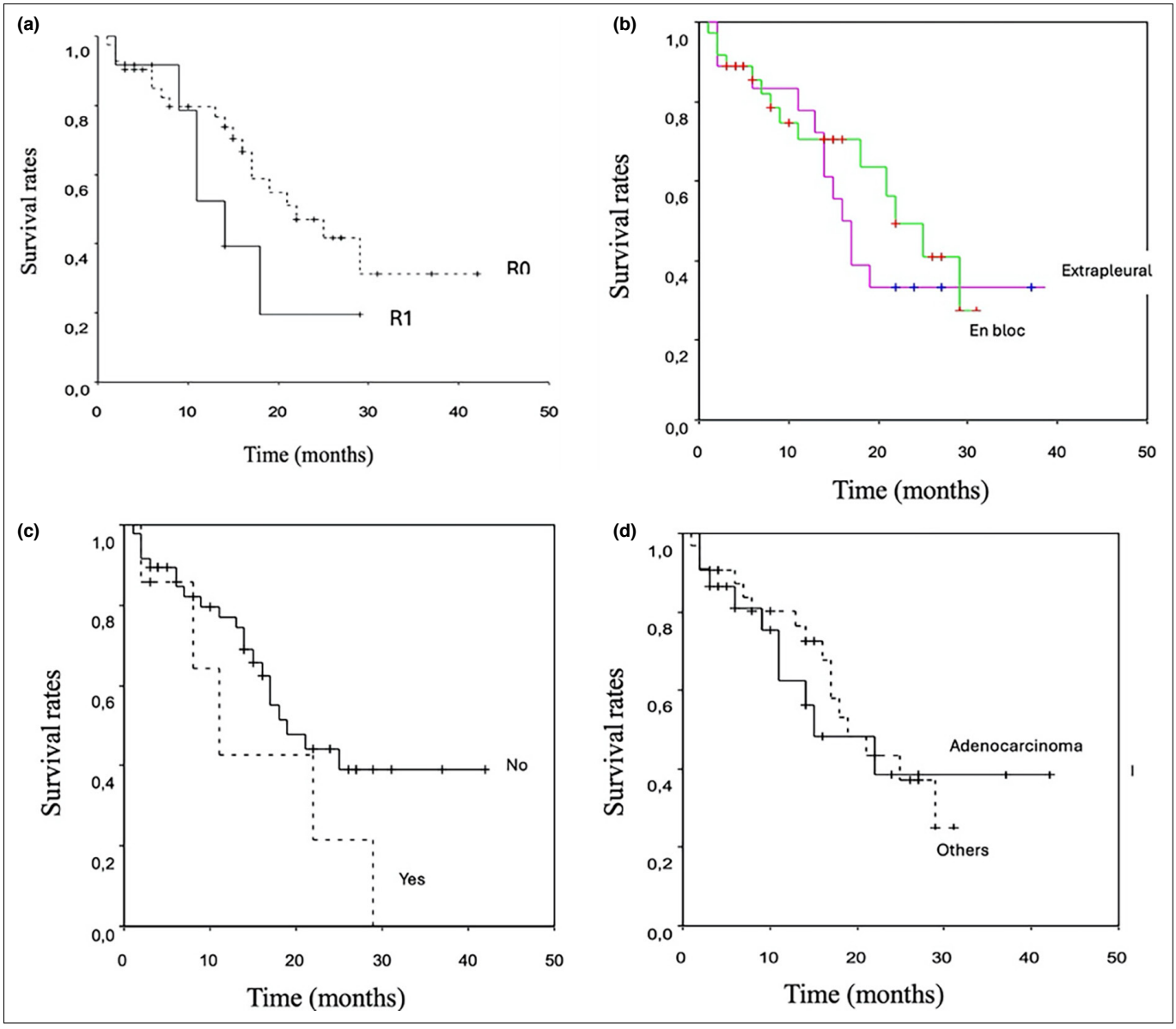

Figure 3: (a) Kaplan-Meier survival curves based on resection margin status (R0 vs. R1). Patients who underwent complete (R0) resection demonstrated a survival advantage over those with incomplete (R1) resection, although the difference was not statistically significant. (b) Kaplan-Meier survival curves comparing en bloc chest wall resection and extrapleural resection. A non-significant trend favoring en bloc resection was observed, suggesting potential oncologic benefits of more radical surgery in selected patients. (c) Kaplan-Meier survival curves stratified by the presence of lymphatic invasion. Patients without lymphatic invasion showed improved survival compared with those with positive lymphatic invasion, although the difference did not reach statistical significance. (d) Kaplan-Meier survival curves comparing adenocarcinoma and non-adenocarcinoma histologies. No significant difference in survival was observed between patients with adenocarcinoma and those with other histological subtypes

outcomes. In terms of surgical technique, patients undergoing en bloc resection demonstrated a trend toward better survival compared with those treated with extrapleural resection (HR: 1.31, 95% CI: 0.85–2.04; p=0.26), although this was not statistically significant [Fig. 2]. Notably, three local recurrences were observed in the extrapleural group, two of which had initially positive surgical margins (R1). These patients subsequently underwent completion surgery.

Multivariate Cox regression analysis was performed to identify independent predictors of survival. Variables with a p-value <0.20 in univariate analysis—including resection margin status, lymphatic invasion, nodal status, age, and chest wall invasion level—were included in the model. Among these, only incomplete resection (R1) remained statistically significant (HR: 1.96, 95% CI: 1.03–3.71; p=0.04). Lymphatic invasion (HR: 1.72, 95% CI: 0.95–3.10; p=0.07) and nodal involvement (N2

Table 2: Univariate and multivariate Cox regression analysis

Variable*	Univariate HR	95% CI	p	Multivariate HR	95% CI	p
Resection margin (R1 vs. R0)	2.1	1.12–3.91	0.12	1.96	1.03–3.71	0.04
Lymphatic invasion (yes vs. no)	1.84	1.00–3.40	0.18	1.72	0.95–3.10	0.07
Nodal status (N2 vs. N0-1)	1.78	0.93–3.38	0.08	1.69	0.89–3.21	0.06
Age (continuous)	1.03	1.00–1.06	0.14	1.02	0.99–1.05	0.08
Chest wall invasion (costal vs parietal pleura)	0.81	0.45–1.45	0.11	0.81	0.45–1.45	0.11
Histologic subtype (adenocarcinoma vs. non-adenocarcinoma)	1.21	0.62–2.36	0.71	–	–	–
Tumor necrosis (yes vs. no)	1.35	0.70–2.59	0.27	–	–	–
Perineural invasion (yes vs. no)	1.48	0.68–3.21	0.65	–	–	–
Adjuvant chemotherapy (yes vs. no)	0.89	0.63–1.28	0.4	–	–	–
Adjuvant radiotherapy (yes vs. no)	1.19	0.88–1.62	0.25	–	–	–
Surgical technique (extrapleural vs. en bloc)	1.31	0.85–2.04	0.26	–	–	–

*: This table summarizes the univariate and multivariate Cox regression results assessing overall survival in non-small cell lung cancer (NSCLC) patients with chest wall invasion. Multivariate analysis was limited to variables with a univariate p-value <0.20 to reduce the risk of overfitting. HR: Hazard ratio, CI: Confidence interval, R0: Complete resection, R1: Incomplete resection

vs. N0-1; HR: 1.69, 95% CI: 0.89–3.21; p=0.06) showed a trend toward worse survival but did not reach statistical significance. These findings are summarized in Table 2 [Fig. 3].

Discussion

This retrospective study contributes to the understanding of prognostic factors in NSCLC patients with chest wall invasion undergoing surgical resection. Our results underscore the importance of achieving complete (R0) resection, which emerged as an independent predictor of improved survival in multivariate analysis. This finding aligns with previous literature emphasizing the critical prognostic impact of negative surgical margins in locally advanced NSCLC.[4,9,13]

Although histopathologic factors such as lymphatic invasion, N2 nodal status, and patient age did not reach statistical significance in multivariate analysis, they demonstrated hazard ratios suggestive of potential prognostic relevance. These trends are consistent with earlier studies indicating poorer outcomes in the presence of lymphovascular invasion and advanced nodal disease.[6–8,12] The lack of statistical significance in our cohort may be attributable to sample size limitations or heterogeneity in treatment strategies.

The five-year survival rate of 29% and the median survival of 19 months observed in our series are in accordance with previously published outcomes for patients with chest wall invasion.[4,10] These figures highlight the ongoing challenges in managing this subgroup, particularly in those with concomitant nodal metastases.

Interestingly, patients with costal invasion demonstrated a trend toward better survival compared with those with isolated parietal pleura involvement, although this difference did not reach statistical significance. This observation may not solely reflect the anatomical site of invasion but rather the surgical approach adopted. Patients with costal involvement in our cohort more frequently underwent en bloc resections, which facilitate radical oncologic clearance and reduce the likelihood of residual disease. Although R1 resections were more frequent in the parietal pleura invasion group, the difference in R1 rates between the two groups was not statistically significant, suggesting that this trend should be interpreted with caution. These findings are consistent with the observations of Batıhan et al.,[4] who reported superior long-term survival in patients undergoing bony chest wall resections, likely due to the lower risk of residual disease.

The choice between extrapleural and full-thickness chest wall resection remains controversial. Some authors advocate for extrapleural dissection to minimize morbidity in cases with limited invasion,[14] whereas others emphasize wider resections to reduce recurrence risk.[9,10,13] In our study, a non-significant increase in local recurrence was observed among patients who underwent extrapleural resection, suggesting a potential trade-off between surgical extent and oncologic adequacy.

Multivariate Cox regression analysis provided further clarity by highlighting the prognostic weight of resection margins, even after adjusting for age, nodal status, and lymphatic invasion. Notably, R1 resection was associated with nearly double the hazard of death compared with R0, reinforcing the need for intraoperative vigilance and margin-oriented surgical strategies.

This study has certain limitations, including its retrospective nature, relatively small sample size, and single-center design, which may limit the generalizability of the findings. Further multicenter prospective studies with larger cohorts are warranted to validate these results.

Conclusion

In conclusion, our study reinforces the clinical importance of complete resection in NSCLC patients with chest wall invasion. While not all histopathologic variables reached statistical significance, their potential prognostic influence should not be overlooked in surgical planning. Achieving R0 resection—preferably via en bloc techniques when feasible—remains a cornerstone of effective treatment, and decisions regarding the extent of resection should be tailored to individual tumor characteristics and intraoperative findings.[4,13,14]

Informed Consent
Due to the retrospective design of the study, patient consent was not obtained.

Conflicts of Interest Statement
The authors have no conflicts of interest to declare.

Funding
The authors declared that this study received no financial support.

Use of AI for Writing Assistance
Artificial intelligence (AI) technology was not used in the preparation of this article.

Author Contributions
Concept – M.F., M.A.B.; Design – M.F., M.A.B.; Supervision – M.F., M.A.B.; Resource – M.F., M.A.B.; Materials – M.F., N.F.; Data Collection and/or Processing - M.F., N.F.; Analysis and/or Interpretation - M.F., N.F.; Literature Review – M.F., N.F.; Writing – M.F., N.F.; Critical Review – M.F., M.A.B.

Acknowledgments
The authors would like to thank the surgical and pathology staff of both participating institutions for their technical assistance in data collection and patient care. Thesis advisor for this study was Associate Professor Mehmet Ali Bedirhan.

Peer-review
Externally peer-reviewed.

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