

## RESEARCH ARTICLE

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# The Prognostic Impact of Supraclavicular Lymph Node Metastases in Lung Cancer: Do We Need a Modification of the Current Staging System?

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### Abstract

**Background:** The management of Stage IIIB non-small-cell lung cancer (NSCLC) is complex. The current staging system does not distinguish between ipsilateral and contralateral supraclavicular lymph node involvement, although this distinction may impact prognosis. This study investigates the differences in prognosis between these two presentations of N3 disease. **Methods:** This study presents a retrospective analysis of 113 patients diagnosed with Stage IIIB NSCLC who had supraclavicular lymph node metastases and underwent chemoradiation therapy. Patients were categorized based on whether their supraclavicular involvement was ipsilateral or contralateral to the primary lung tumor. Survival outcomes were calculated and correlated with various factors. **Results:** Patients with ipsilateral supraclavicular metastases had a median progression-free survival of 12 months, compared to 9 months for those with contralateral involvement. The median overall survival for the two groups was 17 months and 14 months, respectively. Poorer survival outcomes were associated with contralateral nodal involvement, older age, poor performance status, and exclusive radiotherapy treatment. **Conclusion:** Contralateral supraclavicular metastases are associated with a worse prognosis compared to ipsilateral involvement in Stage IIIB NSCLC. These findings suggest a need to reevaluate their classification within current staging systems and to consider systemic treatment for these high-risk patients. Phase III randomized controlled trials are needed to validate this observation.

**Keywords:** Contralateral- NSCLC- Supraclavicular nodal involvement- Survival

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### Introduction

Non-small-cell lung cancer (NSCLC) accounts for 85% of all lung cancers, with the majority being diagnosed at an advanced-stage disease. Among patients with stage I to IV NSCLC, approximately 65% had stage IIIB and IV disease at the time of diagnosis. While stage IV NSCLC is treated with palliative care, stages I to IIIA are potentially curable [1]. In contrast, stage IIIB NSCLC has a very poor prognosis, although some patients can be treated with a combination of chemotherapy, radiotherapy (RT), and surgery. Despite trimodality treatment, overall survival (OS) in stage IIIB NSCLC remains poor [2]. Data addressing stage IIIB prognosis and management are limited, highlighting the need for research to identify prognostic factors and determine the most effective and accurate treatment approaches for these patients.

Establishing guidelines to select patients who benefit from radical therapy and those suitable for palliative care only could help minimize unnecessary toxicities associated with less effective treatments [3].

Lung lymphatics vary according to side. On the right (Rt) lung, the bronchopulmonary lymph nodes drain into the right superior and inferior tracheobronchial lymph nodes, then to the right paratracheal lymph nodes, to the bronchomediastinal trunk, and to the right lymphatic duct. On the left (Lt) side, the superior lobe drains into the left superior and inferior tracheobronchial lymph nodes, then to the left paratracheal lymph nodes, returning to the bronchomediastinal trunk and the thoracic duct. The left inferior lobe of the left lung drains similarly to the superior lobe. Nevertheless, it also drains to the right superior tracheobronchial lymph nodes, then to the same route as the right lung [4].

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Stage III NSCLC represents many challenges in terms of treatment and long-term survival. Surgery does not offer significant oncological benefits, so radiochemotherapy is currently the standard of care for patients with stage IIIB [5]. In the eighth edition of the American Joint Committee on Cancer (AJCC) staging system, stage IIIB was further classified into stage IIIC for patients with N3 disease. Recent changes in the ninth edition of the TNM staging system (TNM-9) include the following: (a) the division of the mediastinal nodal category (N2) into single-station (N2a) and multiple-station (N2b) subcategories as well as (b) the subdivision of multiple extrathoracic metastatic lesions (M1c) into single organ system (M1c1) and multiple organ systems (M1c2) subcategories, with no changes to the N3 disease classification [6].

Previous studies have shown that patients with N3 disease have lower survival rates than those with N1 and N2 diseases, with mean survival time of 19 months for stage III B and 12.6 months for stage III C. On the other hand, stage IIIC prognosis is similar to stage IV disease, with a mean survival time of 12.6 versus 11.5 months; however, the management approach is different. Radiochemotherapy, with a dose of around 60 Gy, has reduced locoregional recurrence. However, administering more than 60 Gy of radiotherapy to patients with N3 disease patients is challenging due to the large target volume and contralateral mediastinal or supraclavicular lymph nodes [7]. Further research is needed to better understand the clinical outcomes for patients at stage IIIC and to investigate the impact of supraclavicular lymph node involvement compared to contralateral lymph node metastases.

The International Association for the Study of Lung Cancer (IASLC) collected a database from 1999 to 2010 for the eighth edition of the TNM classification of lung cancer. These include records of 94,708 patients from Europe, North and South America, Australia, and Asia. Data on the N categorization were available for 31,426 patients. However, the database lacked information regarding the number of involved nodes, and details of the nodal status are limited to the involved nodal station(s) (single vs. multiple). The analysis of this database concluded that the currently used descriptors (N0, N1, N2, N3) are highly prognostic. However, the study was extended to explore if the combination of location and number of involved stations may be helpful in better stratifying patient survival. It was concluded that considering the combination of location, the number of involved stations, and the currently used descriptors correlates to patients' survival [8].

Consequently, it is reasonable to consider further modifications to the current staging system in the N category. The modified staging system should take into account different prognoses, locations, the number of involved stations, skip metastasis, and other associated factors. Additionally, efforts should be made to clearly define the prognosis of stage IIIB with supraclavicular lymph node involvement. Future studies should be directed to accurately determine whether this stage should be categorized and treated as a locoregional stage or be nominated to a higher-risk group. This study is trying to

discuss the prognostic impact of positive supraclavicular lymph nodes on survival and to help answer the unmet debate about whether we should consider patients with contralateral supraclavicular nodal involvement having a higher-risk staging.

## Materials and Methods

This is a multicenter retrospective study on archived patients' files from the four sharing centers in Egypt between 2018 and 2022 (Menoufia University, Ain Shams University, Cairo University, and Suez Canal Authority Hospital). Data were collected from medical records explicitly for this study. Inclusion criteria were pathological evidence of NSCLC and radiological evidence of supraclavicular nodal metastasis. Exclusion criteria were the presence of distant metastasis, poor performance status, inability to fit for antineoplastic treatment, and files missing essential data for the study.

We examined 1,423 files of patients with NSCLC. Out of which, 528 were diagnosed with stage III disease. The high percentage of stage III disease among lung cancer patients can be attributed to the prevalent cultural tendency in the study region for individuals to delay seeking medical attention, often neglecting their symptoms. We found only 113 patients with supraclavicular nodal involvement, fitting the inclusion criteria. Patients were divided into two groups: Group I, those with ipsilateral supraclavicular nodal involvement; Group II, those with contralateral supraclavicular nodal involvement. Patients with both ipsilateral and contralateral involvement were categorized into Group II.

Basic demographic data were collected and tabulated. These included age, sex, smoking history, and performance status by ECOG. Disease characteristics were also collected, including the tumor site (which lung and which lobe), histopathological type, ALK, EGFR, and PDL-1 status. ALK status was described as either wild type or rearranged, and EGFR status was defined as wild or mutant. PDL-1 was considered negative if <1%, low below 50%, and high above 50%.

Treatment: All patients underwent radiotherapy as the primary treatment modality, either as monotherapy or in concurrence with chemotherapy. The concurrent chemotherapy regimen consisted of a cisplatin-based doublet, administered as either a fractionated weekly protocol or a three-weekly protocol. Some patients received induction chemotherapy in the form of platinum-based doublet for 2-3 cycles (cisplatin 75 mg/m<sup>2</sup> day 1 and either pemetrexed 500 mg/m<sup>2</sup> day 1 every 21 days, gemcitabine 1250 mg/m<sup>2</sup> days 1 and 8, or paclitaxel 175 mg/m<sup>2</sup> day 1 with a maximum dose of 300 mg) just for bridging the time gap of radiotherapy waiting list (sequential). Radiotherapy was delivered using an external beam 3D conformal or IMRT technique with a dose of 60–64 Grays (Gy). A standard fractionation of 2 Gy per fraction, five fractions per week, was adopted in all patients. The dose was prescribed so that at least 95% of the planning target volume (PTV) should receive 95% of the dose. In the available imaging modalities (CT, MRI, PET), GTV was defined as all grossly seen

tumor tissue within the lung and lymph nodes. CTV was created by adding a 5–8 mm margin to GTV, including the whole involved nodal station, and then edited to respect anatomical barriers. The internal motion was then assessed, and a margin was added accordingly to create iCTV. PTV was created by adding a 5 mm margin. Matching was done weekly using cone beam CT and daily using KV images.

Patients who received a palliative dose of lung irradiation were excluded. None of the patients received consolidation immunotherapy with durvalumab as it is not reimbursed in the centers where this study was conducted.

The study was approved by the ethical committee of Menoufia University, Faculty of Medicine, with approval number 7/2024TROP18 and in concordance with the Declaration Of Helsinki. Patient consent was not required due to the retrospective observational design of the study.

### Statistical Analysis

The primary endpoint was progression-free survival, calculated from the date of diagnosis to the date of progression or recurrence and analyzed using the Kaplan–Meier method and Cox regression. Similarly, the secondary endpoint was overall survival calculated from the date of diagnosis till the date of death or last follow-up. Data were fed to the computer and analyzed using IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp). Categorical data were represented as numbers and percentages. The chi-square test was applied to compare two groups. Alternatively, when 20% of the cells had an expected count of less than 5, the Fisher exact correction test was used instead, as the chi-square test is unreliable in such cases. Concurrently, continuous data were tested for normality using the Kolmogorov–Smirnov and Shapiro–Wilk tests. Quantitative data were expressed as range (minimum and maximum), mean, standard deviation, median and interquartile range. Student's t-test was employed to compare two groups for normally distributed quantitative variables. The significance of the obtained results was judged at the 5% level.

## Results

The study included 113 patients with stage III NSCLC with supraclavicular involvement, constituting 7.9% of the examined medical records of lung cancer patients. They were divided into two groups: Group I, ipsilateral supraclavicular involvement (75 patients); Group II, contralateral supraclavicular involvement (38 patients).

Both groups were homogeneously balanced in terms of demographics. The median age was 59 years at diagnosis. Males were 61% of patients in Group I and 55% in Group II. About 6.2% only had performance status 3, while other patients had performance status 0, 1, or 2. Right-sided lung tumors were observed in 64% of patients in Group I and 55% in Group II. Patients with upper lobe tumors had more contralateral supraclavicular nodal deposits versus ipsilateral involvement (47.4% versus 22.7%). On the contrary, patients with lower lobe tumors (including the middle lobe of the right lung) had more ipsilateral involvement than contralateral (77% vs. 52%), with a

significant P value of 0.007 (Table 1).

The Kaplan–Meier curve for progression-free survival showed a median PFS of 12 months for patients with ipsilateral nodal involvement vs. 9 months for the contralateral group with a significant p-value of 0.002 (Figure 1 and Table 2a). Cox regression analysis showed a hazard ratio of 1.8 for the contralateral group with  $P = 0.004$ , denoting more risk of contralateral involvement (Table 2b).

Table 1. Comparison between the Two Studied Groups According to Demographic, Pathological, Treatment, and Outcome

	Total (n = 113)	Supraclavicular Ipsilateral (n = 75)	LN metastasis Contralateral (n = 38)
Age (years)			
Min. – Max.	41 – 75	42 – 75	41 – 74
Mean ± SD.	59.14 ± 8.03	59.39 ± 8.01	58.66 ± 8.14
Median (IQR)	59 (53 – 65)	59 (53 – 65.5)	59 (53 – 65)
Sex			
Male	67 (59.3%)	46 (61.3%)	21 (55.3%)
Female	46 (40.7%)	29 (38.7%)	17 (44.7%)
Performance			
0	37 (32.7%)	28 (37.3%)	9 (23.7%)
1	40 (35.4%)	25 (33.3%)	15 (39.5%)
2	29 (25.7%)	17 (22.7%)	12 (31.6%)
3	7 (6.2%)	5 (6.7%)	2 (5.3%)
Smoking	41 (36.3%)	29 (38.7%)	12 (31.6%)
Pathology			
Adenocarcinoma	96 (85.0%)	63 (84.0%)	33 (86.8%)
Squamous	17 (15.0%)	12 (16.0%)	5 (13.2%)
Treatment			
Sequential	31 (27.4%)	18 (24.0%)	13 (34.2%)
CCRT	73 (64.6%)	51 (68.0%)	22 (57.9%)
Radiotherapy	9 (8.0%)	6 (8.0%)	3 (7.9%)
Site primary			
Right	69 (61.1%)	48 (64.0%)	21 (55.3%)
Left	44 (38.9%)	27 (36.0%)	17 (44.7%)
Site lobe			
Upper	35 (31.0%)	17 (22.7%)	18 (47.4%)
Lower	78 (69.0%)	58 (77.3%)	20 (52.6%)
EGFR			
Wild	91 (80.5%)	61 (81.3%)	30 (78.9%)
Mutant	22 (19.5%)	14 (18.7%)	8 (21.1%)
ALK			
Wild	106 (93.8%)	69 (92.0%)	37 (97.4%)
Rearranged	7 (6.2%)	6 (8.0%)	1 (2.6%)
PDL1			
Negative	94 (83.2%)	63 (84.0%)	31 (81.6%)
Low	11 (9.7%)	8 (10.7%)	3 (7.9%)
High	8 (7.1%)	4 (5.3%)	4 (10.5%)
Progressed	101 (89.4%)	67 (89.3%)	34 (89.5%)
Death	76 (67.3%)	47 (62.7%)	29 (76.3%)

CCRT, Concurrent chemoradiation therapy; EGFR, epidermal growth factor receptor; ALK, Anaplastic lymphoma kinase; PDL1, programmed death ligand 1; IQR, Inter quartile range; SD, Standard deviation.

Table 2a. Kaplan-Meier Survival Curve for Progression Free Survival with Supraclavicular LN

	Mean	Median	% End of study	Log rank $\chi^2$	p
Supraclavicular LN					
Ipsilateral	12.16	12	10.70%	10.070*	0.002*
Contralateral	9.553	9	10.50%		

Table 2b. Univariate COX Regression Analysis for Supraclavicular LN Affecting Progression Free Survival (n = 101 vs. 12)

	p	HR (LL – UL 95% C.I)
Supraclavicular LN		
Ipsilateral		1
Contralateral	0.004*	1.841 (1.211 – 2.798)

HR, Hazard ratio; C.I, Confidence interval; LL, Lower limit; UL, Upper Limit; \*, Statistically significant at  $p \leq 0.05$

Similarly, the median overall survival was 17 months for the ipsilateral group compared to 14 months for the contralateral group ( $p < 0.001$ ) with a hazard ratio of 2.18 (Figure 2 and Table 3 a&b).

A multivariate analysis was conducted to determine the independent factors affecting overall survival. Tumor sidedness, whether right or left, did not significantly impact survival ( $p = 0.490$ ). Similarly, no significant impact on survival was observed concerning the tumor site within the lung (upper or lower lobe) ( $p = 0.580$ ). Key negative factors impacting survival included contralateral supraclavicular involvement, older age, and worse performance status with p-values of  $<0.001$ , 0.029, and  $<0.001$ , respectively. Similarly, for factors affecting progression free survival, multivariate analysis revealed that contralateral supraclavicular involvement, older age, and worse performance status were the main negative factors impacting with  $P < 0.001$  for all. Patients

of advanced age and with poor performance status are typically unsuitable for induction chemotherapy or concurrent chemoirradiation, resulting in a poor prognosis, as displayed in Tables 4 and 5.

### Discussion

Supraclavicular lymph nodes can be involved in many types of malignancies. Their anatomical site is easily accessible, facilitating safe biopsy and performing histopathological and molecular tests. These nodes could harbor involvement from breast cancer, lung cancer, lymphoma, or even gastric cancer [9]. Thus, the involvement of supraclavicular lymph nodes in lung cancer is currently under stage 3 disease. The current staging system does not differentiate between ipsilateral and contralateral nodal involvement regarding prognosis and survival. Accordingly, both conditions are treated with the same management plan, usually concurrent chemoirradiation [10].

In this study, we retrospectively analyzed the prognosis of patients with supraclavicular nodal involvement from primary NSCLC. The medical records of 1423 patients were reviewed, and only 7.9% had sole supraclavicular nodal involvement without distant metastasis. Although the incidence of supraclavicular nodal involvement from lung cancer is in the range of 24%–62% [11], it is quite rare to find cases with supraclavicular involvement without having any distant metastasis.

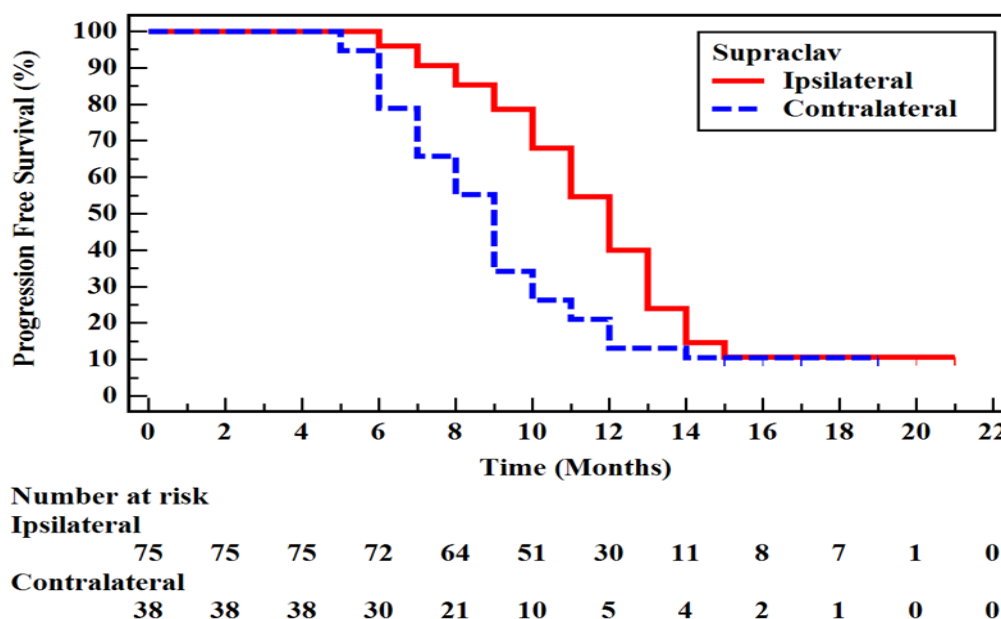


Figure 1. Kaplan-Meier Survival Curve for Progression-Free Survival with Supraclavicular LN.

Table 3a. Kaplan-Meier Survival Curve for Overall Survival with Supraclavicular LN

	Mean	Median	% End of study	Log rank	
				$\chi^2$	p
Supraclavicular LN					
Ipsilateral	17.01	17	30.20%	12.160*	<0.001*
Contralateral	14.07	14	23.40%		

Table 3b. Univariate COX Regression Analysis for Supraclavicular Affecting Overall Survival (n = 76 vs. 37)

	p	HR (LL – UL 95%C.I.)
Supraclavicular LN		
Ipsilateral		1
Contralateral	0.001*	2.184 (1.358 – 3.513)

HR, Hazard ratio; C.I., Confidence interval; LL, Lower limit; UL, Upper Limit; \*, Statistically significant at  $p \leq 0.05$

Although many studies revealed that the median age at diagnosis is about 67–70 years [12], it was 59 years in this study. The incidence was higher in males than females in both studied groups (61% vs. 39% for Group I and 55% vs. 45% for Group II). This matches the results of many studies that have already been published [13]. A possible explanation could be the higher frequency of smoking among males compared to females [14].

In this study, most patients had right-sided lung tumors (64% and 55% for Groups I and II, respectively). Nonetheless, this did not affect survival or prognosis. The

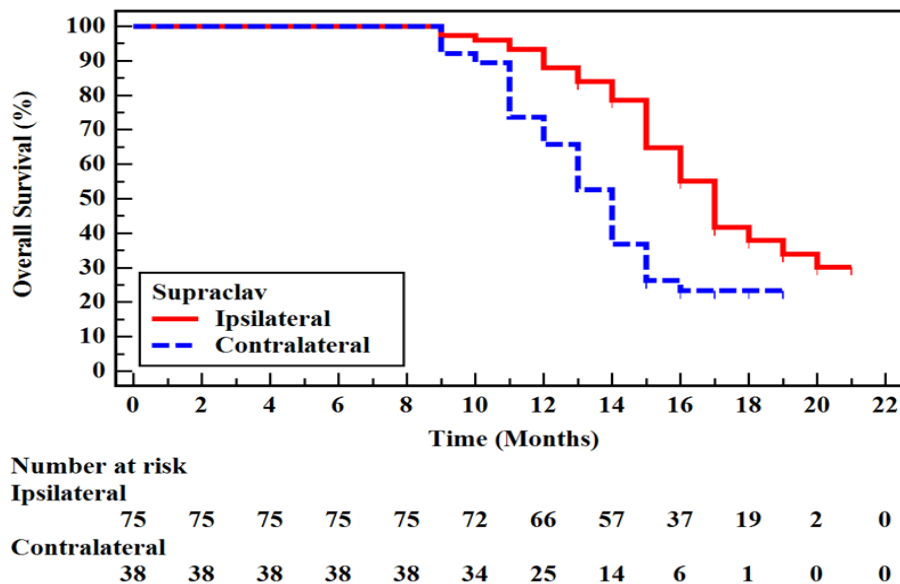


Figure 2. Kaplan-Meier Survival Curve for Overall Survival with Supraclavicular LN

Table 4. Multivariate COX Regression Analysis for the Parameters Affecting Overall Survival (n = 76 vs. 37)

	p	HR (LL – UL 95%C.I.)
Supraclavicular LN [Contralateral]	<0.001*	3.387 (1.904 – 6.023)
Age (years)	0.029*	1.036 (1.004 – 1.070)
Performance	<0.001*	6.117 (4.058 – 9.219)
Treatment		
Sequential	0.532	0.847 (0.503 – 1.426)
CCRT	0.063	2.953 (0.944 – 9.236)
Radiotherapy		1
Site primary [Left]	0.49	0.839 (0.510 – 1.380)
Site lobe [Upper]	0.58	1.168 (0.674 – 2.026)

CCRT, Concurrent chemoradiation therapy; HR, Hazard ratio; C.I., Confidence interval; LL, Lower limit; UL, Upper Limit; \*, Statistically significant at  $p < 0.05$

Table 5. Multivariate COX Regression Analysis for the Parameters Affecting Progression-Free Survival (n = 101 vs. 12)

	p	HR (LL – UL 95%C.I.)
Supraclavicular LN [Contralateral]	<0.001*	4.001 (2.416 – 6.626)
Age (years)	<0.001*	1.079 (1.047 – 1.112)
Performance	<0.001*	4.495 (3.175 – 6.364)
Treatment		
Sequential	0.734	1.208 (0.407 – 3.586)
CCRT	1	1.000 (0.372 – 2.690)
Radiotherapy		1
Site primary [Left]	0.422	0.841 (0.551 – 1.284)
Site lobe [Upper]	0.907	1.027 (0.652 – 1.618)

CCRT, Concurrent chemoradiation therapy; HR, Hazard ratio; C.I., Confidence interval; LL, Lower limit; UL, Upper Limit; \*, Statistically significant at  $p < 0.05$

regression analysis of survival yielded a p-value of 0.335, indicating no significant effect of tumor sidedness on survival, in contrast to findings observed in colon cancer. Likewise, a meta-analysis by Myra van Laar reported the same finding by analyzing 12 studies on the effects of tumor location on prognosis [15].

Interestingly, tumors within the upper lobe of the lung had more frequent contralateral supraclavicular involvement (47% vs. 23%) than those in the lower lobe or middle lobe in the case of the right lung (52% versus 77%). This may be attributed to the skip metastasis through the subclavian vessels near upper lobe tumors. However, this observation had no impact on survival. The tumor site within a particular lobe was found to be worse in the case of lower lobe tumors in a SEER database [16]. However, this was not the case in this study, probably due to the strict selection criteria that were applied.

The primary aim of this study was to evaluate the impact of laterality of supraclavicular involvement on prognosis. Thus, survival analysis was done for PFS and OS, comparing both groups. It was found that patients with ipsilateral supraclavicular involvement had a median PFS of 12 months and a median OS of 17 months. This was statistically higher than those of patients with contralateral involvement with a median PFS and OS of 9 and 14 months, respectively. The hazard ratio was 1.84 for PFS and 2.18 for OS. This result confirms the hypothesis that contralateral supraclavicular involvement is more dangerous than ipsilateral ones. Given its negative impact on both PFS and OS, contralateral supraclavicular involvement may warrant a staging category different from ipsilateral involvement after validating these observations in phase III trials.

The one-year OS in unresectable stage III NSCLC is about 56%–58%. The median overall survival is estimated to be 14–17 months [12]. These numbers are almost identical to the outcomes in this study. Another study by Matthew Evison reported that median OS can be extended to 26 months if surgery is added. However, they reported PFS to be 9 to 12 months [17].

In another study, the median OS was estimated to be between 20–30 months [18]. This wide range of survival outcomes between different studies denotes that further subgroups within stage III NSCLC may be worrisome of independent categorization and may have different management plans. In support of this hypothesis, prolonged overall survival was observed with systemic treatment but not immunotherapy.

Median overall survival was reported to be in the range of 23 months in a recent study involving immunotherapy as part of the treatment protocol for recruited patients [19]. However, trials that were designed to detect the benefit of immunotherapy per se showed a much longer duration of response. It was within the range of 48 months in the Pacific Trial [20]. The median was not even reached in other studies, with 71% of patients alive at 24 months of follow-up [21].

Contradictingly, a study on 204 patients focused on supraclavicular nodal status as a prognostic factor. It did not show any survival difference between patients with supraclavicular involvement and those without.

However, this study did not investigate the laterality of the supraclavicular nodes. The median PFS was in the range of 9 months, and OS was in the range of 34 months [22].

In the current study, the median OS was much lower, which may be explained by the nonavailability of good treatment options upon progression. This is confirmed by the identical duration of PFS in both studies. However, immunotherapy and many targeted agents are not reimbursed upon progression in this study's center.

To the best of our knowledge, this is the first study to specifically search into the laterality of supraclavicular nodal involvement in NSCLC. The difference in outcomes between both groups should raise our attention to the need to modify the staging system and possibly the treatment algorithm depending on laterality. As this clinical situation (supraclavicular involvement without distant metastasis) is relatively rare, further more extensive studies should be conducted to validate our results.

A key limitation of our study is the absence of durvalumab consolidation therapy, which has become the standard of care for patients with stage III NSCLC following concurrent chemoradiotherapy. This omission inevitably limits the direct generalizability of our findings to contemporary clinical practice. However, it is important to note that neither study arm received durvalumab, thereby preserving the internal validity and balance of the comparison between ipsilateral and contralateral supraclavicular lymph node metastasis. Our primary endpoint was sufficient to reject the null hypothesis and demonstrate the prognostic distinction under investigation. While future studies incorporating durvalumab are warranted to confirm the applicability of these results in the current treatment era, our findings remain robust in addressing the specific prognostic question posed.

In conclusion, NSCLC with isolated supraclavicular nodal involvement is a rare clinical situation. Patients with contralateral supraclavicular involvement have a worse prognosis than those with ipsilateral involvement. Tumor sidedness (right or left) and location (upper or lower lobe) did not impact survival differently. Modifying the current staging system is needed to better categorize patients with contralateral involvement and potentially incorporate systemic treatment into their management at a later stage.

## Author Contribution Statement

All authors made significant contributions to the work presented. A.S.: collection of data and writing the manuscript; H.S.: collection of data and writing the manuscript; M.M.: data analysis; N.E.: registration of the study, interpretation of statistical results, and journal submission; U.A.: collection of data and writing the manuscript; M.A.: collection of data and writing the manuscript. All authors gave final approval for the version to be published, chose the journal to which the article was submitted, and agreed to be responsible for all aspects of the work.

## Acknowledgements

### Ethical approval

The study was approved by the ethical committee of Menoufia University, Faculty of Medicine, with approval number 7/2024TROP18 and in concordance with the Declaration Of Helsinki. Patient consent was not required due to the retrospective observational design of the study.

### Availability of data and material

All data generated or analyzed during this study are included in this published article.

### Conflicts of Interest

All authors declare no conflicts of interest.

### Abbreviations

AJCC: American Joint Committee on Cancer  
 ALK: Anaplastic lymphoma kinase  
 CCRT: Concurrent chemoradiation therapy  
 CTV: Clinical target volume  
 ECOG: Eastern Cooperative Oncology Group  
 EGFR: Epidermal growth factor receptor  
 GTV: Gross target volume  
 Gy: Gray  
 IASL: International Association for the Study of Lung Cancer  
 IMRT: Intensity-modulated radiotherapy  
 NSCLC: Non-small-cell lung cancer  
 OS: Overall survival  
 PDL1: Programmed death ligand 1  
 PTV: Planning target volume  
 PFS: Progression-free survival  
 RT: Radiotherapy.

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