



# Benefits of adjuvant chemotherapy in elderly patients with stage IB–IIIB non-small cell lung cancer: a propensity-matched analysis

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**Background:** Adjuvant chemotherapy (ACT) is a well-recognized and well-established treatment for surgically resected non-small cell lung cancer (NSCLC), but its suitability for elderly patients remains controversial. Further investigation is warranted to guide ACT decisions in this demographic.

**Methods:** We extracted data from the Surveillance, Epidemiology, and End Results (SEER) database, focusing on patients aged 70 years or older who underwent surgical resection for stage IB, II, or III NSCLC as per the 7th edition of the American Joint Committee on Cancer staging system (AJCC 7th edition). Propensity score matching (PSM), Kaplan-Meier analysis, and Cox regression were employed for statistical analyses.

**Results:** There were 503 participants received ACT in this study of 2,000 patients aged 70 or older with stage IB–IIIB NSCLC who underwent surgical resection without preoperative chemotherapy. Overall, ACT did not significantly correlate with extended overall survival (OS) ( $P=0.07$ ) compared to non-ACT. After 2:1 PSM, the matched cohort comprised 317 non-ACT and 206 ACT recipients. Post-PSM, the ACT group exhibited improved OS ( $P=0.044$ ) compared to the non-ACT group. Cox regression analysis identified gender, primary tumor site, histologic grade, N stage, and ACT as independent predictors of OS ( $P<0.05$ ). Subgroup analysis indicated amplified ACT benefits in individuals aged 70–79 years, male, with N1 stage, or those without radiotherapy.

**Conclusions:** ACT may confer benefits to elderly stage IB–IIIB NSCLC patients, particularly those aged 70–79 years, male, and with N1 stage.

**Keywords:** Non-small cell lung cancer (NSCLC); chemotherapy; survival; stage IB–IIIB; propensity-matched analysis

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## Introduction

With an estimated two million new cases and 1.76 million deaths per year, lung cancer is one of the most commonly diagnosed cancers and the leading cause of cancer-related

deaths worldwide (1). Non-small cell lung cancer (NSCLC) accounts for approximately 85% of all lung cancers (2). Although surgery is the most effective curative treatment option for patients with NSCLC, some patients experience

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recurrence beyond the surgical margin even after receiving curative surgery (3).

In this day and age of targeted therapy and immunotherapy, cytotoxic chemotherapy is still used to treat operable NSCLC (4). Adjuvant chemotherapy (ACT) is used to prevent recurrence in patients who have had their NSCLC completely removed (5). According to national and local guidelines, ACT should be considered for stage IB disease and is strongly recommended for stages II and IIIA disease (6). The Lung Adjuvant Cisplatin Evaluation (LACE)-meta-analysis, which included mainly randomized clinical trials comparing ACT *vs.* observation in 4,584 patients undergoing surgical resection for early-stage disease, revealed a significant but modest 5.4% improvement in the chemotherapy arm's 5-year survival rate, implying that we must "treat many to save few" in our daily practices (7,8). Improving patient selection is an important goal of ongoing chemotherapy trials because not all patients require ACT, but selecting those who will benefit remains difficult (9).

In actual practice, oncologists are more likely to believe that older patients cannot endure chemotherapy or that the survival advantage of ACT is not worth the hazards to these patients. According to SEER-Medicare database research, oncologists are increasingly giving ACT to patients aged 70–79 years in response to current guideline

recommendations. However, physicians are still hesitant to use ACT on patients aged 80 years and older. The study demonstrated that between 2004 and 2011, the 5-year overall survival (OS) for patients in the 70–79 years age group improved by 7.6% with an increase in the use of ACT. The 5-year OS for patients over 80 years improved by just 1.0% (10). It is yet to be shown whether the rise in 5-year survival is the result of more ACT administered. As a result, further research to guide ACT choices in older NSCLC patients is required. We present this article in accordance with the STROBE reporting checklist (available at <https://tcr.amegroups.com/article/view/10.21037/tcr-24-2/rc>).

## Methods

### *Patient selection and data source*

Data from the Surveillance, Epidemiology, and End Results (SEER) database were collected using SEER\*Stat software from patients aged 70 years or older, with surgical resection, no preoperative chemotherapy, and pathologically confirmed stage IB, II, or III NSCLC as per the 7th edition American Joint Committee on Cancer staging system (AJCC 7th edition) (version 8.4.0.1; National Cancer Institute, USA). The following were the inclusion criteria: (I) diagnosed with lung cancer by histology between 2010 and 2015; (II) 70 years of age or older; (III) undergoing surgical resection; and (IV) without preoperative chemotherapy. The following were the exclusion criteria: (I) with more than one malignant tumor; (II) small cell carcinoma; (III) tumor-node-metastasis (TNM) stage of IA or IV; (IV) T stage of TX or NA; (V) N stage of NX or N3. After screening, 2,000 eligible patients were eventually included into the analysis. The data processing procedure is depicted in *Figure 1*. Because SEER is a publicly accessible database, the Institutional Review Board of Zhongshan Hospital Qingpu Branch assessed this study and determined that it was exempt from ethical review. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

### *Variables to investigate*

Age, gender, race, laterality, primary tumor site, pathological type, histological grade, T stage, N stage, surgery, scope of regional lymph node removed (SRLNR), radiotherapy, chemotherapy, OS, and survival months were collected. Based on their treatment, patients were separated into ACT

### Highlight box

#### Key findings

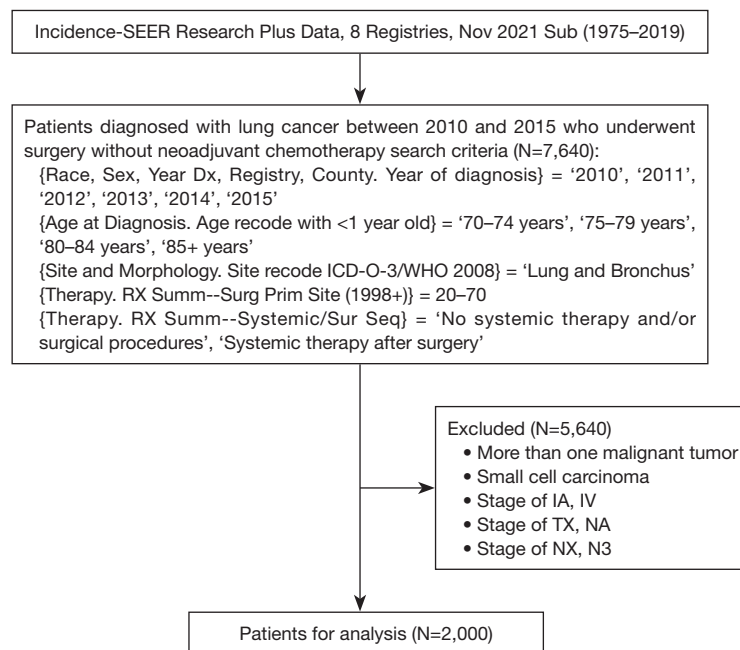
- Adjuvant chemotherapy (ACT) may confer survival benefits to elderly patients with stage IB–IIIB non-small cell lung cancer (NSCLC).
- Subgroup analysis revealed that ACT was particularly beneficial for individuals aged 70–79 years, male, and with N1 stage NSCLC.

#### What is known and what is new?

- ACT is a standard treatment option for surgically resected NSCLC, but its efficacy in elderly patients has been debated.
- This study demonstrates that ACT may offer survival advantages in elderly patients with NSCLC, especially in certain subgroups such as those aged 70–79 years and with N1 stage disease.

#### What is the implication, and what should change now?

- Clinicians should consider ACT as a potential treatment option for elderly patients with stage IB–IIIB NSCLC, particularly those meeting the criteria identified in this study.
- Further research and clinical trials are warranted to validate these findings and refine patient selection criteria for ACT in the elderly NSCLC population.



**Figure 1** Patient screening flowchart. SEER, Surveillance, Epidemiology, and End Results; WHO, World Health Organization.

and non-ACT groups. This study's primary outcome was OS. It was described as the period of time between the date of discovery and the date of death, whatever the cause.

### Propensity score matching (PSM)

Treatment-related selection bias in retrospective cohort studies is unavoidable due to an imbalance in baseline characteristics. PSM can eliminate selection bias, compensate for differences in clinical characteristics across groups, and strengthen the findings of retrospective cohort research (11). To balance the baseline features of the ACT and non-ACT groups, the current study used a logistic regression model using propensity scores. The dependent variable was designated as ACT, whereas the covariables were various baseline characteristics. The PSM was carried out in a 1:2 ratio using closest neighbor matching and a caliper of 0.001. To compare baseline characteristics between groups, chi-squared or Fisher's exact tests were utilized.

### Statistical analysis

R version 4 was used for the analyses. For survival analysis, Kaplan-Meier methods and log-rank tests were utilized. Cox proportional hazards regression was used for univariate and multivariate analyses. Variables from the univariate

analysis with  $P < 0.05$  were selected for multivariate analysis. Differences of  $P < 0.05$  were considered statistically significant.

## Results

### Baseline characteristics

This research involved 2,000 patients aged 70 years or older with stage IB–IIIB NSCLN receiving surgical resection without preoperative chemotherapy. In total, 1,497 patients (74.85%) did not receive ACT, whereas 503 patients (25.15%) did. The patients' baseline characteristics are displayed in *Table 1*. Age ( $P < 0.001$ ), pathological type ( $P = 0.004$ ), histological grade ( $P < 0.001$ ), T stage ( $P < 0.001$ ), N stage ( $P < 0.001$ ), and radiation ( $P < 0.001$ ) showed significant differences in the unmatched cohort between the ACT and non-ACT groups. The matched cohort included 206 patients who received ACT and 317 patients who did not. In the matched cohorts, the baseline characteristics were well-balanced between the ACT and non-ACT groups. *Figure 2* depicts the propensity score distribution map and histogram before and after matching.

### Survival analysis

Kaplan-Meier analysis revealed no statistically significant

**Table 1** Comparison of the clinical and pathological characteristics between non-ACT and ACT groups before and after PSM

Characteristics	Before PSM			After PSM		
	Non-ACT (n=1,497)	ACT (n=503)	P value	Non-ACT (n=317)	ACT (n=206)	P value
Age (years), n (%)			<0.001			0.76
70–79	1,061 (70.9)	450 (89.5)		290 (91.5)	186 (90.3)	
≥80	436 (29.1)	53 (10.5)		27 (8.5)	20 (9.7)	
Gender, n (%)			0.52			>0.99
Female	768 (51.3)	249 (49.5)		165 (52.1)	108 (52.4)	
Male	729 (48.7)	254 (50.5)		152 (47.9)	98 (47.6)	
Race, n (%)			0.50			0.47
White	1,233 (82.4)	404 (80.3)		280 (88.3)	176 (85.4)	
Black	75 (5.0)	31 (6.2)		13 (4.1)	8 (3.9)	
Other	189 (12.6)	68 (13.5)		24 (7.6)	22 (10.7)	
Laterality, n (%)			0.32			0.38
Left	621 (41.5)	222 (44.1)		122 (38.5)	88 (42.7)	
Right	876 (58.5)	281 (55.9)		195 (61.5)	118 (57.3)	
Tumor site, n (%)			>0.99			0.48
Lung lobe	1,431 (95.6)	481 (95.6)		307 (96.8)	201 (97.6)	
Main bronchus	6 (0.4)	2 (0.4)		0 (0.0)	1 (0.5)	
Overlapping	28 (1.9)	9 (1.8)		6 (1.9)	3 (1.5)	
Unknown	32 (2.1)	11 (2.2)		4 (1.3)	1 (0.5)	
Pathological type, n (%)			0.004			0.79
Adenocarcinoma	526 (35.1)	206 (41.0)		116 (36.6)	76 (36.9)	
Squamous cell carcinoma	483 (32.3)	124 (24.7)		82 (25.9)	58 (28.2)	
Other	488 (32.6)	173 (34.4)		119 (37.5)	72 (35.0)	
Histological grade, n (%)			<0.001			0.43
I	210 (14.0)	40 (8.0)		39 (12.3)	18 (8.7)	
II	695 (46.4)	219 (43.5)		137 (43.2)	94 (45.6)	
III	483 (32.3)	208 (41.4)		125 (39.4)	81 (39.3)	
IV	23 (1.5)	7 (1.4)		6 (1.9)	2 (1.0)	
Unknown	86 (5.7)	29 (5.8)		10 (3.2)	11 (5.3)	
T stage, n (%)			<0.001			0.57
T1	64 (4.3)	81 (16.1)		23 (7.3)	20 (9.7)	
T2	1,072 (71.6)	254 (50.5)		207 (65.3)	123 (59.7)	
T3	285 (19.0)	125 (24.9)		73 (23.0)	52 (25.2)	
T4	76 (5.1)	43 (8.5)		14 (4.4)	11 (5.3)	

**Table 1** (continued)

Table 1 (continued)

Characteristics	Before PSM		P value	After PSM		P value
	Non-ACT (n=1,497)	ACT (n=503)		Non-ACT (n=317)	ACT (n=206)	
N stage, n (%)			<0.001			0.09
N0	1,212 (81.0)	178 (35.4)		220 (69.4)	126 (61.2)	
N1	188 (12.6)	180 (35.8)		71 (22.4)	53 (25.7)	
N2	97 (6.5)	145 (28.8)		26 (8.2)	27 (13.1)	
Surgery, n (%)			0.08			0.22
Sublobectomy	261 (17.4)	71 (14.1)		33 (10.4)	19 (9.2)	
Lobe or bilobectomy	1,187 (79.3)	408 (81.1)		281 (88.6)	181 (87.9)	
Pneumonectomy	49 (3.3)	24 (4.8)		3 (0.9)	6 (2.9)	
SRLNR, n (%)			0.17			0.54
None	126 (8.4)	33 (6.6)		16 (5.0)	12 (5.8)	
<4	159 (10.6)	41 (8.2)		25 (7.9)	14 (6.8)	
≥4	1,154 (77.1)	411 (81.7)		271 (85.5)	173 (84.0)	
Others	58 (3.9)	18 (3.6)		5 (1.6)	7 (3.4)	
Radiotherapy, n (%)			<0.001			0.34
No	1,435 (95.9)	384 (76.3)		308 (97.2)	196 (95.1)	
Yes	62 (4.1)	119 (23.7)		9 (2.8)	10 (4.9)	

ACT, adjuvant chemotherapy; PSM, propensity score matching; SRLNR, scope of region lymph node removed.

difference in the OS of patients who received ACT *vs.* those who did not ( $P=0.07$ ) (Figure 3A). The median OS for the ACT and non-ACT groups was 56 months [95% confidence interval (CI): 47–65] and 49 months (95% CI: 45–53), respectively. The ACT and non-ACT groups had 3- and 5-year OS of 62.28% *vs.* 58.74% and 47.86% *vs.* 43.66%, respectively. After 1:2 matching, patients who received ACT had a longer OS than non-ACT patients ( $P=0.044$ ) (Figure 3B). The median OS for the ACT and non-ACT groups was 67 months (95% CI: 56–106) and 48 months (95% CI: 42–71), respectively. The ACT and non-ACT groups' 3- and 5-year OS were 65.37% *vs.* 59.38% and 53.66% *vs.* 45.91%, respectively.

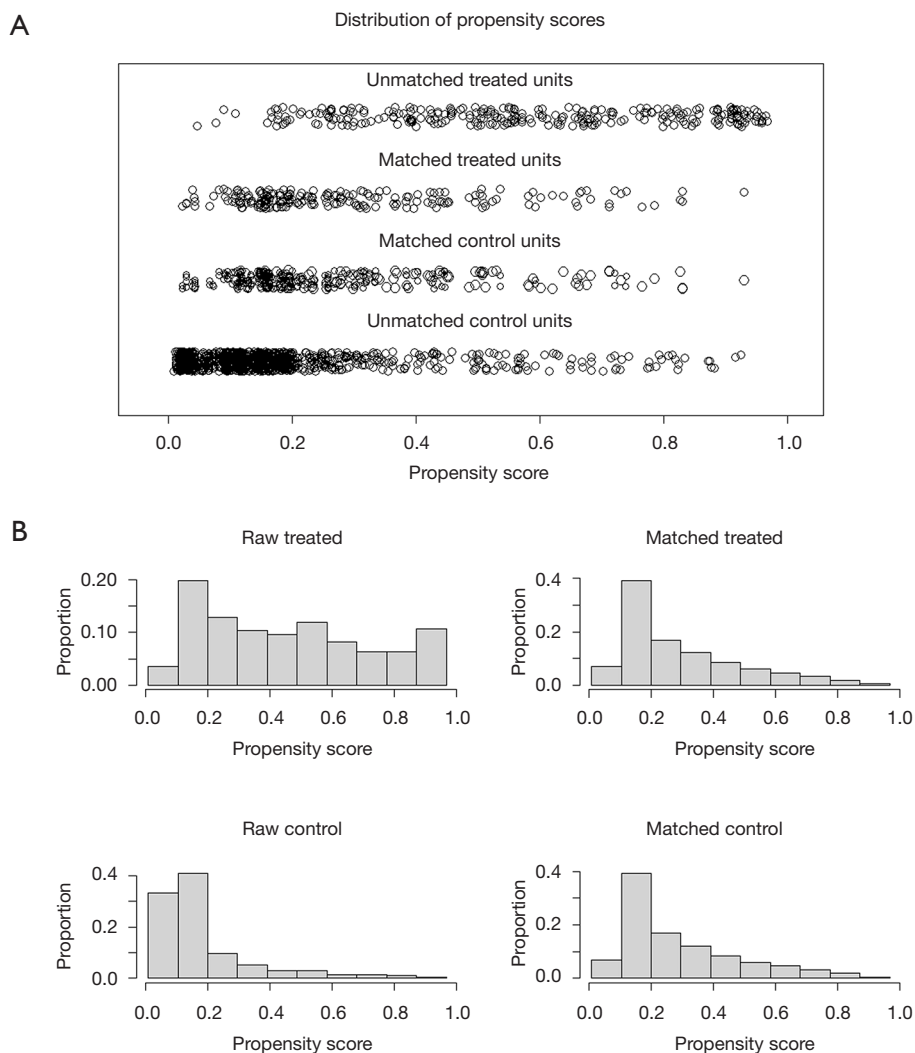
#### Univariate and multivariate Cox regression analyses after PSM

Age, gender, primary tumor site, histological grade, N stage, radiotherapy, and ACT were all significantly associated with OS ( $P<0.05$ ) (Table 2). Variables from the univariate analysis with  $P<0.05$  were considered for multivariate

analysis. Gender, primary tumor site, histological grade, N stage, and ACT were shown to be independently linked with OS ( $P<0.05$ ) in the multivariate analysis. In relation to gender, females were used as the control group, while men [hazard ratio (HR) =1.42; 95% CI: 1.13–1.79;  $P=0.003$ ] were identified as an adverse prognostic factor for OS. N1 (HR =1.72; 95% CI: 1.3–2.26;  $P<0.001$ ) and N2 (HR =3.33; 95% CI: 2.3–4.82;  $P<0.001$ ) exhibited a negative prognostic impact on OS in comparison to N0. ACT was linked to a higher life expectancy ( $P=0.002$ ).

#### Subgroup analysis after PSM

Subgroup analyses stratified by age and N stage were performed using Kaplan-Meier. When the age range was 70–79 years, the ACT group had a longer OS than the non-ACT group. The 3- and 5-year OS of the ACT and non-ACT groups was 67.03% *vs.* 60.8% and 55.27% *vs.* 47.1%, respectively ( $P=0.03$ ) (Figure 4A). There was not a significant difference in the OS of the ACT and non-ACT groups when the age was  $\geq 80$  years. The 3- and 5-year OS



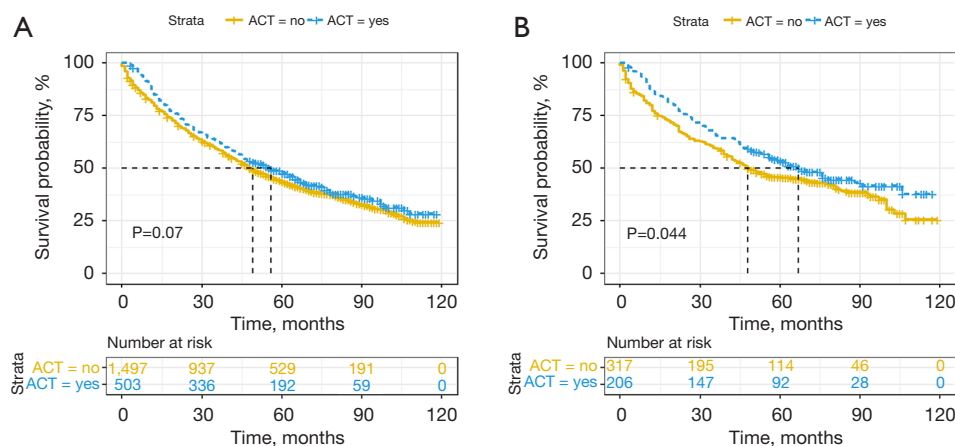
**Figure 2** Distribution map (A) and histogram (B) of the propensity score before and after matching. Treated, ACT; control, non-ACT. ACT, adjuvant chemotherapy.

of the ACT and non-ACT groups was 50% vs. 44.44% and 38.6% vs. 33.33%, respectively ( $P=0.96$ ) (Figure 4B). In patients with N0, there was no significant difference in OS between the ACT and non-ACT groups, with 3-year OS rates of 70.41% vs. 68.55% and 5-year OS rates of 57.74% vs. 55.24% ( $P=0.58$ ) (Figure 5A). Conversely, among patients with N1, the ACT group had a 3- and 5-year OS of 71.7% and 57.97%, respectively, compared to 44.43% and 28.51% in the non-ACT group ( $P<0.001$ ) (Figure 5B). Furthermore, for patients with N2, although there was a trend toward better OS in the ACT group, the difference was not statistically significant, with respective 3-year OS of 29.63% vs. 23.08% and 5-year OS of

25.93% vs. 15.38% ( $P=0.08$ ) (Figure 5C). Cox proportional hazard analysis was used to investigate the survival benefit of ACT for patients in various categories. ACT improved the OS of patients who were 70–79 years of age (HR =0.76; 95% CI: 0.59–0.98;  $P=0.03$ ), male (HR =0.72; 95% CI: 0.52–1;  $P=0.048$ ), lung lobes (HR =0.78; 95% CI: 0.61–0.99;  $P=0.04$ ), N1 stage (HR =0.42; 95% CI: 0.26–0.68;  $P<0.001$ ), and non-radiotherapy (HR =0.75; 95% CI: 0.59–0.96;  $P=0.02$ ) (Figure 6).

## Discussion

Randomized controlled studies of patients with stage I–



**Figure 3** Kaplan-Meier curves of elderly patients with stage IB–IIIb NSCLC undergoing surgical resection without preoperative chemotherapy before (A) and after (B) PSM. ACT, adjuvant chemotherapy; NSCLC, non-small cell lung cancer; PSM, propensity score matching.

**Table 2** Univariate and multivariate analysis of variables for OS after PSM

Characteristics	Univariate analysis		Multivariate analysis	
	HR (95% CI)	P value	HR (95% CI)	P value
Age (years)				
70–79	1		1	
≥80	1.61 (1.13–2.29)	0.008	1.12 (0.77–1.62)	0.56
Gender				
Female	1		1	
Male	1.37 (1.09–1.72)	0.007	1.42 (1.13–1.79)	0.003
Race				
White	1			
Black	1.09 (0.64–1.86)	0.76		
Other	0.66 (0.42–1.03)	0.07		
Laterality				
Left	1			
Right	1.03 (0.81–1.3)	0.82		
Tumor site				
Lung lobe	1		1	
Main bronchus	7.32 (1.02–52.7)	0.048	13.98 (1.76–111.01)	0.01
Overlapping lesion of lung	1.52 (0.72–3.22)	0.27	1.66 (0.77–3.55)	0.19
Unknown	1.24 (0.4–3.88)	0.71	1.83 (0.58–5.8)	0.30

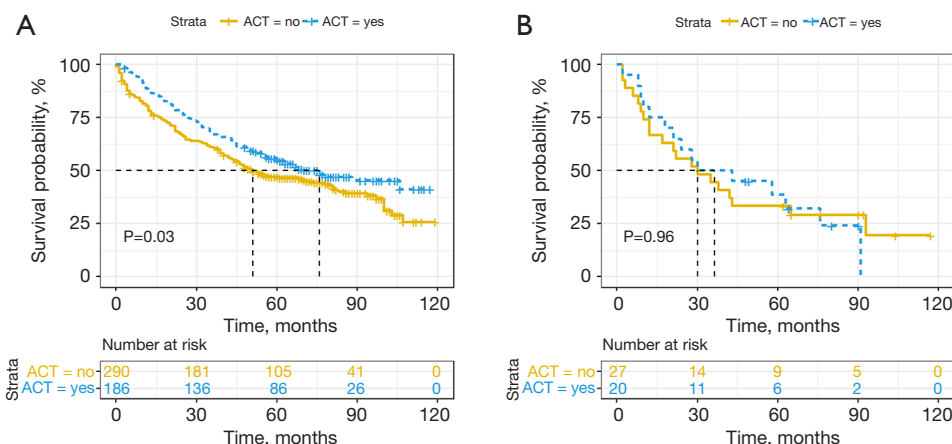
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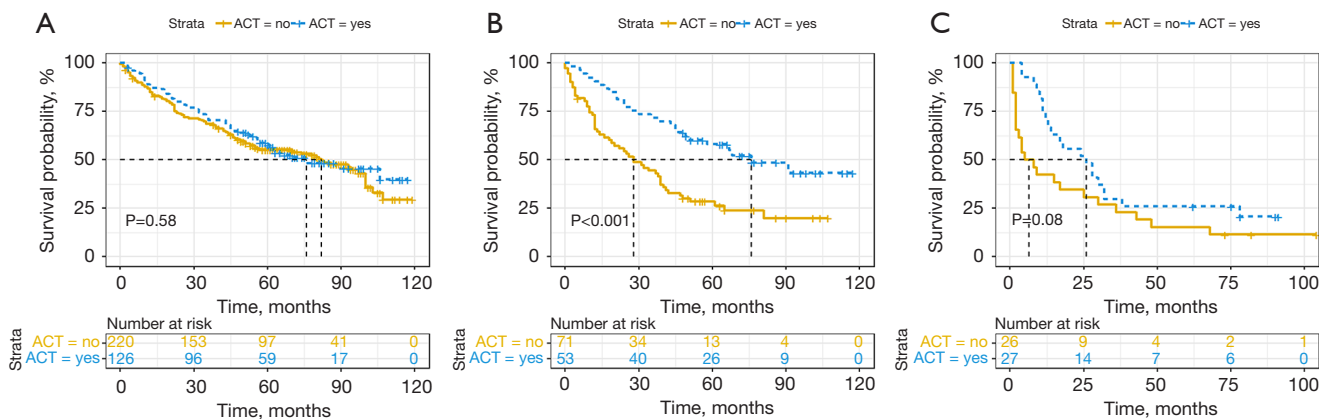
Characteristics	Univariate analysis		Multivariate analysis	
	HR (95% CI)	P value	HR (95% CI)	P value
Pathological type				
Adenocarcinoma	1			
Squamous cell carcinoma	1.11 (0.84–1.48)	0.46		
Other	0.93 (0.71–1.22)	0.61		
Histological grade				
I	1		1	
II	1.04 (0.68–1.58)	0.86	0.88 (0.57–1.35)	0.55
III	1.59 (1.05–2.4)	0.03	1.39 (0.91–2.12)	0.13
IV	5.02 (2.18–11.58)	<0.001	5.55 (2.34–13.16)	<0.001
Unknown	1.22 (0.61–2.46)	0.58	1.29 (0.64–2.61)	0.48
T stage				
T1	1			
T2	0.88 (0.57–1.35)	0.55		
T3	1.3 (0.82–2.07)	0.26		
T4	0.79 (0.39–1.59)	0.51		
N stage				
N0	1		1	
N1	1.53 (1.17–2)	0.002	1.72 (1.3–2.26)	<0.001
N2	2.96 (2.12–4.14)	<0.001	3.33 (2.3–4.82)	<0.001
Surgery				
Sublobectomy	1			
Lobe or bilobectomy	0.8 (0.56–1.16)	0.24		
Pneumonectomy	0.79 (0.31–2.03)	0.63		
SRLNR				
None	1			
<4	0.9 (0.49–1.65)	0.73		
≥4	0.8 (0.5–1.29)	0.36		
Others	0.85 (0.37–1.95)	0.70		
Radiotherapy				
No	1		1	
Yes	2.7 (1.65–4.42)	<0.001	1.49 (0.86–2.57)	0.15
ACT				
No	1		1	
Yes	0.78 (0.62–0.99)	0.044	0.68 (0.53–0.86)	0.002

OS, overall survival; PSM, propensity score matching; HR, hazard ratio; CI, confidence interval; SRLNR, scope of regional lymph node removed; ACT, adjuvant chemotherapy.





**Figure 4** Kaplan-Meier survival curves comparing the ACT and non-ACT groups when age was 70–79 years (A) or ≥80 years (B) after PSM. ACT, adjuvant chemotherapy; PSM, propensity score matching.

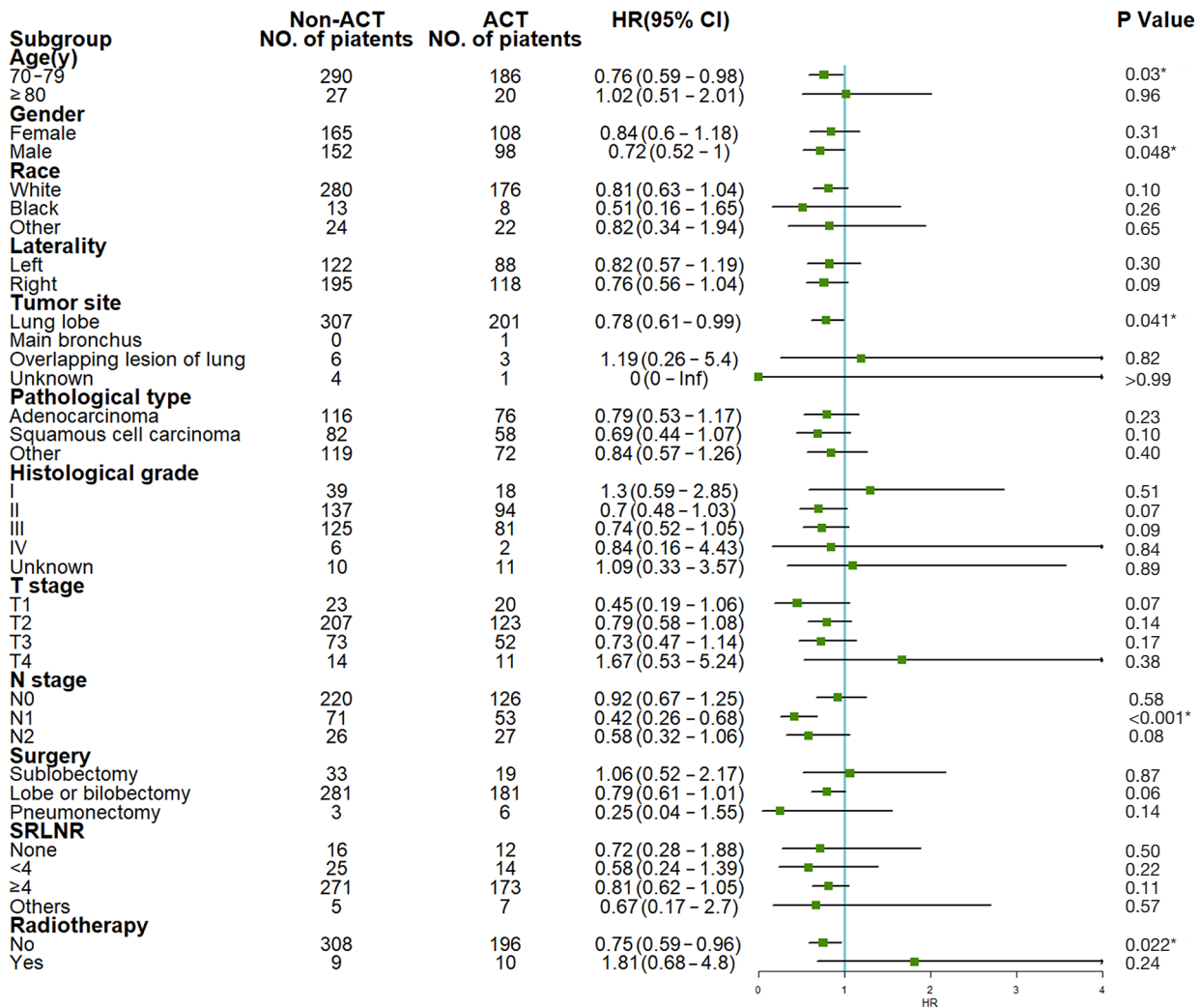


**Figure 5** Kaplan-Meier survival curves comparing the ACT and non-ACT groups when the N stage was N0 (A), N1 (B), or N2 (C) after PSM. ACT, adjuvant chemotherapy; PSM, propensity score matching.

III NSCLC have shown that postoperative cisplatin-based treatment considerably lowers the risk of mortality, particularly in stage II and III cancer (12,13). ACT with a cisplatin-based combination regimen is the present treatment standard in stage II and IIIA NSCLC following surgical resection (14,15). Postoperative ACT is also recommended by the National Comprehensive Cancer Network (NCCN) for stage IB patients with high-risk criteria such as poorly differentiated tumors, vascular invasion, wedge resection, visceral pleural invasion (VPI), and uncertain lymph node status (16). Nonetheless, the applicability of ACT to the elderly has been questioned due to their shorter life expectancy. It is critical for older patients to examine both the long-term advantages of

ACT and the hazards associated with short-term toxicity. These dangers make deciding whether ACT is beneficial challenging (17). According to one study, early mortality with ACT following full resection of NSCLC was greater in individuals over the age of 70 years (18). For these reasons, it is critical to investigate the effect of ACT on the OS of elderly stage IB–IIIB NSCLC patients.

A meta-analysis of randomized trials found that patients over the age of 70 with NSCLC benefited from ACT in the same way as their younger counterparts (19). Another recent trial found that ACT enhanced the prognosis following routine lung cancer surgery in people over the age of 75 years with stage IB–IIIA NSCLC (17). Before PSM, our investigation found that ACT did not substantially



**Figure 6** Forest plots summarizing HRs of ACT in subgroup analyses after PSM. \*, P<0.05. ACT, adjuvant chemotherapy; HR, hazard ratio; CI, confidence interval; SRLNR, scope of regional lymph node removed; PSM, propensity score matching.

enhance the OS of patients aged 70 years or older with stage IB–IIIB NSCLC. Differences in clinicopathological parameters, such as age, gender, race, tumor location, pathological type, histological grade, T stage, N stage, surgical procedures, SRLNR, and radiotherapy, must be considered. In the adjusted cohorts, baseline characteristics were identical across the ACT and non-ACT groups after PSM, and patients with ACT had a longer OS than those without. Subgroup analysis stratified by age revealed that ACT enhanced the OS of those 70–79 years old with stage IB–IIIB NSCLC. When the participants were over 80 years old, there was no significant difference in OS between the ACT and non-ACT groups. As a result, the maximum age

for ACT is may be 80 years old.

A lobectomy with mediastinal lymph node dissection is the usual treatment modality for lung cancer. Because of its high local control, the operation has been demonstrated to be better than a sublobar resection such as a wedge resection or a segmentectomy (20,21). The NCCN classifies sublobar resection as a high-risk characteristic and a sign of ACT (16). Patients receiving sublobar resection have a higher risk of insufficient lymphadenectomy and positive margins (22). Lymph node assessment is critical for appropriate staging and therapy. The key to effective adjuvant therapy administration is precise staging. ACT, for example, is advised for NSCLC patients who have any

evidence of lymph node metastasis, and the advantages of ACT in patients with node-positive NSCLC have been thoroughly documented. Furthermore, the therapeutic benefits of ACT on any undetected residual cancer may contribute to reduced recurrence risk and enhanced survival (23). According to a recent study, ACT was not advantageous to patients with stage T1a to T1c tumors with insufficient nodal evaluation, but it might be used as a supplemental treatment for patients with stage T2a tumors who were stated to have node-negative cancer but were probably understaged (24). In our study, however, the surgical approach and extent of lymph node dissection had no influence on the prognosis of patients aged 70 years or older with stage IB–IIIB NSCLC. In our research, neither sublobectomy nor insufficient lymph node dissection were associated with ACT benefits. As a result, we hypothesize that sublobectomy and insufficient lymph node dissection are unimportant factors in predicting ACT for older NSCLC patients and that R0 resection may be the most significant consideration for elderly NSCLC patients.

In NSCLC patients, tumor stage has been routinely utilized to predict prognosis and guide ACT (25,26). A high T stage always indicates a poor prognosis and may necessitate adjuvant treatment. In individuals with node-negative NSCLC, a tumor size greater than 4 cm is regarded as an indication for ACT (27). We discovered no ACT benefit in patients with high T. In our study, patients with N1 had greater OS after adjuvant treatment. Toubat *et al.* discovered that N1 NSCLC patients treated with ACT had a 14% 5-year survival advantage over those receiving surgery alone, indicating that N1 NSCLC patients may benefit more than previously thought from ACT (28,29).

Many studies found that women with NSCLC had considerably superior OS (30,31). We also found a comparable effect of gender on OS in individuals aged 70 years or older with stage IB–IIIB NSCLC. On the contrary, male patients in our research had an improved OS as a result of ACT, but female patients did not. Previous research has found that postoperative radiation is ineffective and appears to be related to higher toxicity in older individuals with early-stage NSCLC (32). In our study, those who had radiation had a poorer prognosis, and ACT did not enhance the prognosis. Patients who did not receive radiation had a superior outcome after ACT.

There are various limitations to our study. First, because this is retrospective research, the population selection is bound to be biased, and it cannot control for confounding factors as rigorously as prospective studies. Although we

performed the PSM to lessen the potential bias, there may be an undiscovered bias that the PSM did not correct (33). Following that, it is unclear how patients in the SEER database are chosen for various therapies. Finally, the SEER database is unable to give more precise information on performance status, surgical margin status, chemotherapy regimens and cycles, and additional treatment after recurrence, so we must proceed with caution. As a result, additional prospective randomized controlled studies are required to confirm our findings.

## Conclusions

Finally, our study discovered that ACT may give survival advantages to elderly stage IB–IIIB NSCLC patients. Consideration may be given to a potential upper age limit of 80 years for ACT. ACT is more beneficial to patients at the N1 stage. ACT benefits male patients more than female ones. T stage, pathological type, histological grade, surgical approach, and SRLNR, on the other hand, may not be significant in identifying whether ACT was beneficial. Radiotherapy is not advised for older NSCLC patients who are undergoing surgery. Clinicians should carefully assess if ACT is helpful for elderly patients with advanced NSCLC.

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## Footnote

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appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

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