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Sublobar resection versus lobectomy for patients with stage T1-2N0M0 pulmonary typical carcinoid tumours: a population-based propensity score matching analysis

Hao Yang and Tonghua Mei *

Department of Respiratory and Critical Care Medicine, The First Affiliated Hospital of Chongqing Medical University, Chongqing Medical University, Chongqing, China

* Corresponding author. Department of Respiratory and Critical Care Medicine, The First Affiliated Hospital of Chongqing Medical University, No. 1 You Yi Road, Chongqing 400016, China. Tel: +86-18983466333; fax: +86-23-89012017; e-mail: mtonghua@163.com (T. Mei).

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Key question

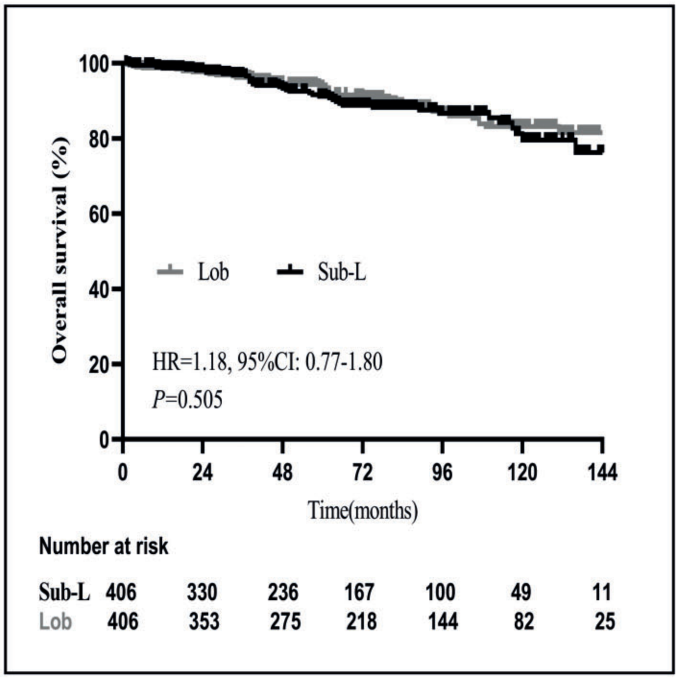
Which is the optimal surgical approach for stage T1-2N0M0 pulmonary typical carcinoid tumours?

Key finding(s)

Sublobar resection showed similar overall survival compared to lobectomy (5-year OS=90.78% versus 93.30%; HR 1.18, 95% CI: 0.77-1.80; P=0.505).

Take-home message

In this population-based cohort, we demonstrated that sublobar resection was not inferior to lobectomy in terms of overall survival for stage T1-2N0M0 pulmonary typical carcinoid tumours.



Abstract

OBJECTIVES: It is widely accepted that surgical resection of localized pulmonary typical carcinoid (TC) tumours remains the primary curative modality. However, the optimal extent of resection remains controversial. This study aimed to investigate the survival rates of patients with stage T1-2N0M0 TC tumours who underwent sublobar resection or lobectomy.

METHODS: We queried the Surveillance, Epidemiology, and End Results database for patients who underwent surgery after being diagnosed with stage T1-2N0M0 TCs from 2004 to 2016. Propensity score matching (PSM) analysis was used to equalize the baseline characteristics between the sublobar resection group and the lobectomy group. Kaplan–Meier analysis and the Cox proportional hazard model were performed for survival analysis.

RESULTS: Of the 2469 patients included, 658 (26.65%) underwent sublobar resection and 1811 (73.35%) underwent lobectomy. All 2469 patients were analysed with PSM and, following PSM, 812 patients were included in the final analysis and divided into 2 groups of 406 patients. In the matched cohort, Kaplan–Meier analysis demonstrated no significant difference in survival curves between the sublobar resection and lobectomy groups in patients with stage T1-2N0M0 TC tumours [5-year overall survival (OS) = 90.78% vs 93.30%; hazard ratio 1.18, 95% confidence interval: 0.77–1.80; $P = 0.505$]. Subgroup analysis by tumour size showed that the sublobar resection group was identical to the lobectomy group in OS for tumours ≤3.0 cm. In addition, no difference in OS between surgical groups was observed in any subgroups. In the multivariable Cox analysis, age ≤65 years, female sex, married status and adequate lymph node assessment (≥5) were associated with improved OS, whereas the extent of resection was not.

CONCLUSIONS: Sublobar resection seems to be associated with similar survival to lobectomy for stage T1-2N0M0 TC tumours if lymph node assessment is performed adequately. This analysis suggests that sublobar resection should be considered an appropriate alternative for stage T1-2N0M0 TC tumours. However, further validations are needed in large, multicentre prospective studies.

Keywords: Pulmonary typical carcinoid • Sublobar resection • Lobectomy • Propensity score matching analysis • SEER database

ABBREVIATIONS

ACs	Atypical carcinoids
CI	Confidence interval
HR	Hazard ratio
LNs	Lymph nodes
NSCLC	Non-small-cell lung cancer
OS	Overall survival
PCs	Pulmonary carcinoids
PSM	Propensity score matching
SEER	Surveillance, Epidemiology, and End Results
TCs	Typical carcinoids

INTRODUCTION

Pulmonary carcinoids (PCs), histopathologically categorized as typical carcinoids (TCs) and atypical carcinoids (ACs), are rare and indolent neuroendocrine tumours that account for about 1–2% of pulmonary neoplasms [1–3]. TC, which accounts for >80% of PC, often occurs in a central location and is generally associated with lower risks of lymph node metastasis and distant metastasis and a better prognosis than AC [1, 4–6].

TC has poor sensitivity to radiotherapy and chemotherapy, is mainly treated by surgery and is associated with 90–97% 5-year overall survival (OS) with surgical resection [5, 7–9]. Currently, National Comprehensive Cancer Network and European Neuroendocrine Tumour Society guidelines recommend surgical resection as the primary and the most effective therapy for operable localized TC patients who can tolerate surgery with good performance status and adequate pulmonary reserve, as it has been regarded as a curative treatment [10]. Surgery aims to remove the lesion completely and maximally preserve normal lung tissue. Lobectomy and sublobar resection (segmental resection and wedge resection) are the major surgical approaches for resectable lung tumours. Traditionally, lobectomy is accepted as the standard surgical procedure for early-stage non-small-cell lung cancer (NSCLC), while sublobar resection is regarded as an alternative for patients with limited pulmonary function [11, 12]. However, due to relatively low rates of disease recurrence, metastasis and death, as well as the rarity of these tumours and the lack of prospective studies, no global consensus exists on the optimal extent of surgery for TC. This study aimed to compare sublobar resection from lobectomy in patients with stage T1-2N0M0 TC tumours and has been configured according to the STROBE checklist [13].

PATIENTS AND METHODS

Data sources

The data used for the present study were extracted from the Surveillance, Epidemiology, and End Results (SEER) database. The dataset collects registry information, including patient survival, disease stage and treatment from different geographic regions for ∼35% of the US population [14]. We have been given access to the database with the reference number 10281-Nov2019 by SEER*Stat 8.3.8. Because individual patient data were de-identified in the SEER database, approval from an ethics committee or institutional review board was not required.

Study population

Patients aged ≥18 years who were diagnosed between 2004 and 2016 with pathologically confirmed stage T1-2N0M0 pulmonary TC tumours (histologic codes 8240) were enrolled. Those who underwent lobectomy and sublobar resection (including segmental resection and wedge resection) were included, while those with lymph node metastasis, distant metastases, an unknown number of examined lymph nodes (LNs), or missing tumour size and stage information were excluded. ACs (including patients with preoperative diagnoses of TCs, which were changed to ACs by postoperative pathological examination) were excluded. Patients with a diagnosis at autopsy or death were excluded, as were patients with a history of other primary cancers. TCs that originated from the main bronchus were excluded because these cases probably received bronchial resection.

The following patient characteristics were retrospectively reviewed: clinical and pathological characteristics, therapy information and survival data, including age at diagnosis, laterality, marital status, sex, race, histologic grade, primary tumour site, the number of LNs examined, tumour size, radiotherapy, adjuvant chemotherapy, survival months and vital status. The TNM staging was based on the criteria described in the 8th edition of the *American Joint Committee on Cancer (AJCC) Staging Manual*.

Outcome

The primary end point was OS; OS was defined as the time from surgery to death from any cause, and patients alive were censored at the time of the last recording. The follow-up duration was calculated from 2004 to 2016.

Table 1: Baseline characteristics before and after propensity score matching, *n* (%)

Characteristics	Before propensity score matching				After propensity score matching		
	Total	Sub-L (*N* = 658)	Lob (*N* = 1811)	*P*-Value	Sub-L (*N* = 406)	Lob (*N* = 406)	*P*-Value
Mean age ± SD, years	57.81 ± 14.12	61.95 ± 11.99	56.31 ± 14.53	<0.001	59.95 ± 12.39	60.66 ± 14.05	0.201
Sex				0.300			1.000
Female	1772 (71.77)	462 (70.21)	1310 (72.34)		292 (71.92)	292 (71.92)	
Male	697 (28.23)	196 (29.79)	501 (27.66)		114 (28.08)	114 (28.08)	
Race				0.310			0.940
White	2202 (89.19)	578 (87.84)	1624 (89.67)		356 (87.68)	353 (86.95)	
Black	164 (6.64)	52 (7.90)	112 (6.18)		30 (7.39)	31 (7.64)	
Others	103 (4.17)	28 (4.26)	75 (4.14)		20 (4.93)	22 (5.42)	
Marital status				0.035			0.991
Married	1525 (61.77)	391 (59.42)	1134 (62.62)		248 (61.08)	251 (61.82)	
Single	334 (13.53)	78 (11.85)	256 (14.14)		51 (12.56)	49 (12.07)	
Separated	492 (19.93)	151 (22.95)	341 (18.83)		90 (22.17)	88 (21.67)	
Unknown	118 (4.78)	38 (5.78)	80 (4.42)		17 (4.19)	18 (4.43)	
Laterality				0.949			0.831
Left	988 (40.02)	264 (40.12)	724 (39.98)		169 (41.63)	166 (40.89)	
Right	1481 (59.98)	394 (59.88)	1087 (60.02)		237 (58.37)	240 (59.11)	
Primary tumour site				0.128			0.896
Upper lobe, lung	858 (34.75)	210 (31.91)	648 (35.78)		140 (34.48)	136 (33.50)	
Middle lobe, lung	490 (19.85)	127 (19.30)	363 (20.04)		77 (18.97)	82 (20.20)	
Lower lobe, lung	1010 (40.91)	282 (42.86)	728 (40.20)		175 (43.10)	169 (41.63)	
Overlapping lesion of lung	25 (1.01)	9 (1.37)	16 (0.88)		2 (0.49)	3 (0.74)	
Lung, NOS	86 (3.48)	30 (4.56)	56 (3.09)		12 (2.96)	16 (3.94)	
Grade				0.917			0.961
I	865 (35.03)	235 (35.71)	630 (34.79)		135 (33.25)	141 (34.73)	
II	165 (6.68)	44 (6.69)	121 (6.68)		25 (6.16)	25 (6.16)	
III/IV	36 (1.46)	8 (1.22)	28 (1.55)		5 (1.23)	4 (0.99)	
Unknown	1403 (56.82)	371 (56.38)	1032 (56.99)		241 (59.36)	236 (58.13)	
Mean number of LNs involved ± SD	6.46 ± 6.89	2.30 ± 4.80	7.98 ± 6.90	<0.001	3.57 ± 5.73	3.84 ± 3.98	0.434
Tumour size				<0.001			0.544
0–3.0 cm	2163 (87.61)	637 (96.81)	1526 (84.26)		385 (94.83)	381 (93.84)	
3.1–5.0 cm	306 (12.39)	21 (3.19)	285 (15.74)		21 (5.17)	25 (6.16)	
Radiotherapy				0.626			0.704
No	2450 (99.23)	652 (99.09)	1798 (99.28)		402 (99.01)	403 (99.26)	
Yes	19 (0.77)	6 (0.91)	13 (0.72)		4 (0.99)	3 (0.74)	
Adjuvant chemotherapy				0.714			0.806
No	2435 (98.62)	648 (98.48)	1787 (98.67)		398 (98.03)	397 (97.78)	
Yes	34 (1.38)	10 (1.52)	24 (1.33)		8 (1.97)	9 (2.22)	

LNs: lymph nodes; Lob: lobectomy; NOS: not otherwise specified; SD: standard deviation; Sub-L: sublobar resection.

Statistical analysis

Patients were classified into 2 groups based on the surgical approach: a lobectomy group and a sublobar resection group. Propensity score matching (PSM) was employed using 1:1 nearest neighbour matching with a calliper of 0.03 to equalize baseline characteristics between cohorts. A logistic regression model that included age, laterality, marital status, sex, race, histologic grade, primary tumour site, the number of LNs examined, tumour size, radiotherapy and adjuvant chemotherapy was used for the PSM. Comparisons between continuous variables were performed using paired *t*-tests or the non-parametric Wilcoxon signed-rank test. Frequencies (percentages) were calculated for categorical variables and McNemar's tests were adopted to compare between cohorts. The Kaplan–Meier method was used to plot the survival curve with a log-rank test to evaluate survival difference. Variables with $P < 0.20$ in the univariable analysis were entered into in the multivariable analysis. Cox proportional hazards models were used to identify factors associated with OS. *P*-values <0.05 were considered statistically significant. Due to the exploratory nature of the study, no adjustment was made for multiple comparisons. Analyses were performed using SPSS version 26, GraphPad Prism 8.0.2 and R version 3.5.0.

RESULTS

Baseline characteristics

A total of 2469 eligible patients were included, of whom 1811 (73.35%) underwent lobectomy and 658 (26.65%) underwent sublobar resection. The patient demographics and clinical characteristics are summarized in Table 1. The mean age of the whole cohort was 57.81 ± 14.12 years. The mean number of LNs examined was 6.46 (±6.89), and at least 50.99% of patients had an examined lymph node number ≥5. The majority of patients were white (89.19%), female (71.77%) and married (61.77%). The median follow-up time was 73 months. The 3-, 5- and 10-year OS was 96.57%, 93.57% and 85.52%, respectively.

Distributions in age ($P < 0.001$), tumour size ($P < 0.001$) and the number of LNs examined ($P < 0.001$) were significantly different in the lobectomy group and the sublobar resection group

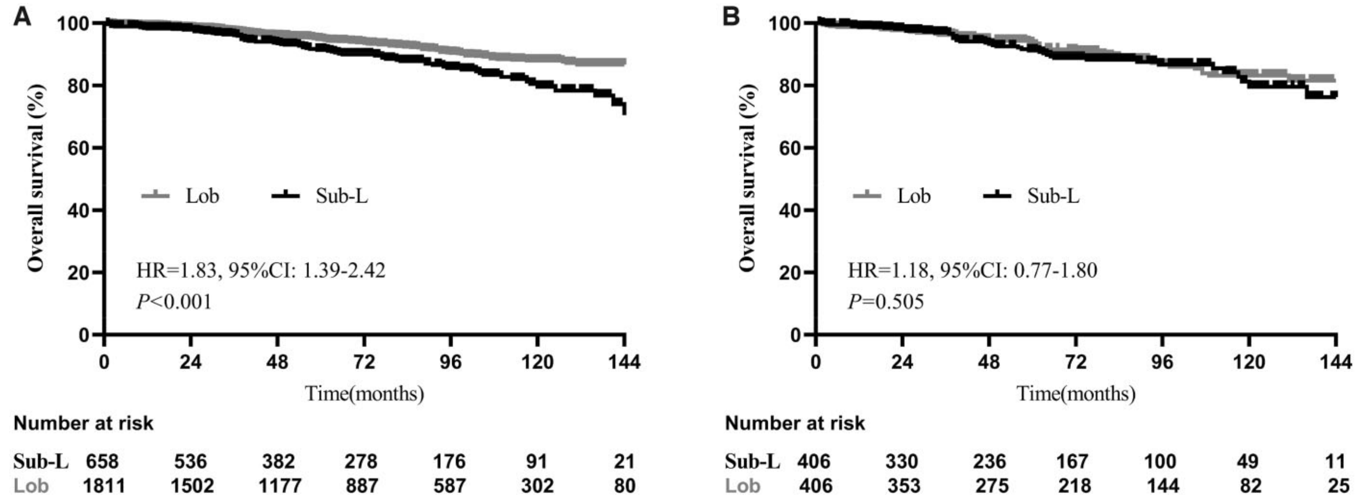


Figure 1: Kaplan–Meier survival curve of stage T1-2N0M0 typical carcinoids. (**A**) Sublobar resection versus lobectomy in typical carcinoids before propensity score matching. (**B**) Sublobar resection versus lobectomy in typical carcinoids after propensity score matching. Lob: lobectomy; Sub-L: sublobar resection.

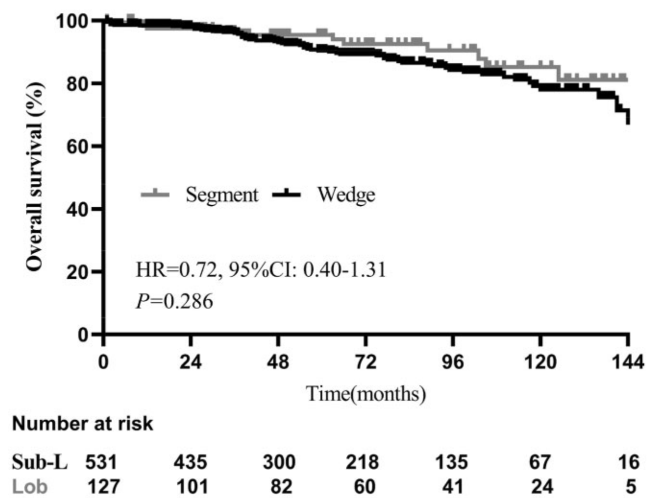


Figure 2: Kaplan–Meier survival curve of sublobar resection versus lobectomy in stage T1-2N0M0 typical carcinoids stratified by tumour size after propensity score matching. (**A**) Sublobar resection versus lobectomy in the ≤1-cm group. (**B**) Sublobar resection versus lobectomy in the 1 cm < $T \le 2$ cm group. (**C**) Sublobar resection versus lobectomy in the 2 cm < $T \le 3$ cm group. Sub-L: sublobar resection, Lob: lobectomy.

(Table 1). Compared to patients in the sublobar resection group, patients who underwent lobectomy were more likely to be younger and to have larger tumours and had a higher proportion of LNs dissected. Therefore, we performed PSM among all 2469 patients. After PSM, 812 patients were included in the final analysis and divided into 2 groups of 406 patients. In the final analytical model, all factors, including age, tumour size and the number of LNs examined, were well-balanced between groups.

Survival analysis

The Kaplan–Meier curve showed that sublobar resection had a worse OS before PSM [5-year OS = 90.60% vs 94.61%; 10-year OS = 78.84% vs 87.77%; hazard ratio (HR) = 1.83, 95% confidence interval (CI): 1.39–2.42; $P < 0.001$; Fig. 1A], but no survival difference was noted after PSM (5-year OS = 90.78% vs 93.30%; 10-year OS = 79.18% vs 82.95%; HR = 1.18, 95% CI: 0.77–1.80; $P = 0.505$; Fig. 1B). In the sublobar resection group, 127 patients underwent segmental resection and 531 received wedge resection. There was no significant difference between segmental resection and wedge resection in terms of OS (5-year OS = 95.42% vs 89.40%; 10-year OS = 85.19% vs 77.11%; HR = 0.72, 95% CI: 0.40–1.31; $P = 0.286$; Fig. 2).

Subgroup analysis

In the subgroup analysis by tumour size, there was no significant difference between lobectomy and sublobar resection in the $T \le 1$ cm group (HR = 0.76; 95% CI, 0.32–1.81; $P = 0.537$; Fig. 3A), the 1 cm < $T \le 2$ cm group (HR = 1.14; 95% CI, 0.65–2.00; $P = 0.653$; Fig. 3B) or the 2 cm < $T \le 3$ cm group (HR = 1.58; 95% CI, 0.51–4.84; $P = 0.426$; Fig. 3C). Because the number in the $T > 3$ cm group was small, statistical analysis was not applied. To further compare survival with different variable factors, an additional exploratory subgroup analysis was performed. The Cox proportional hazard model was used to depict the forest plot. The results showed that there was no significant difference in survival between the lobectomy group and the sublobar resection group across all the analysed subgroups, including age, sex, race, marital status, laterality and the number of LNs examined (Fig. 4).

Univariable and multivariable analyses

The univariable analysis of relevant variables affecting OS can be seen in Table 2. In the multivariable analysis, after adjusting for sex, age, primary tumour site, marital status, the number of LNs examined and adjuvant chemotherapy, there was no significant difference between sublobar resection and lobectomy in terms of OS (HR, 1.17; 95% CI, 0.83–1.44; $P = 0.369$) (Table 2).

DISCUSSION

Recently, with increased routine medical examinations and technical improvements in diagnostic imaging, the detection rate of TCs has gradually increased [1, 2, 14]. Surgery is currently the mainstay of potentially curative treatment for TCs. Unfortunately,

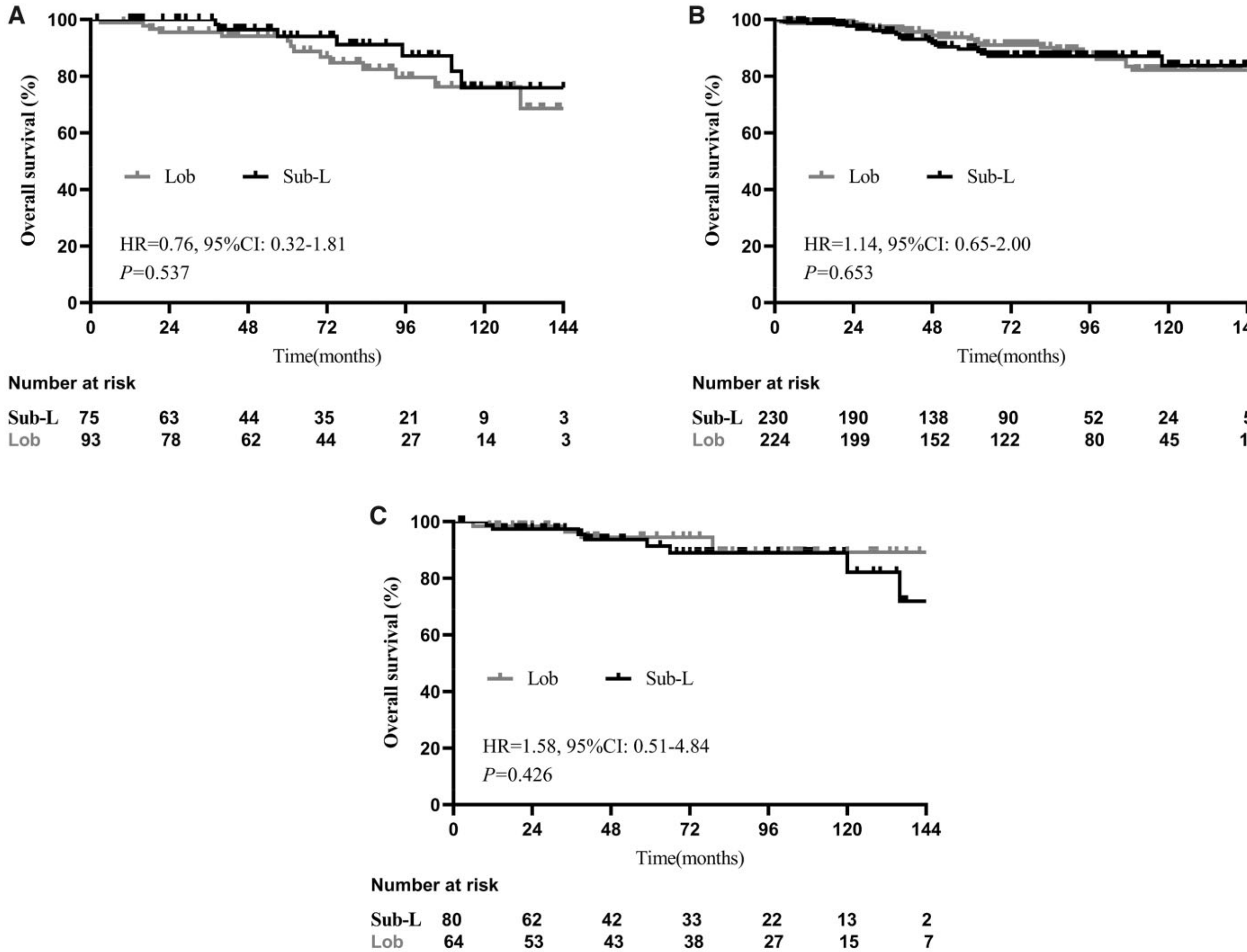


Figure 3: Kaplan–Meier survival curve of wedge resection vs segmental resection in typical carcinoids. Segment: segmental resection; Wedge: wedge resection.

there is no clear consensus on the appropriate surgical approach for early-stage TCs. Some prior studies have demonstrated that sublobar resection is comparable to lobectomy for PC tumours [5, 15–19]. Yendamuri *et al.* [18]. showed that extent of resection was not associated with OS for TC tumours and concluded that sublobar resection in patients with TC tumours was a reasonable alternative to lobectomy as long as complete resection with negative margins and adequate mediastinal staging was performed. Furqan *et al.* [5]. reported that the 5-year survival rate following sublobar resection was comparable to that following lobectomy for either localized ($P = 0.209$) or regional ($P = 0.364$) TC tumours. In addition, Fox *et al.* [17]. showed that sublobar resection is associated with non-inferior disease-specific survival and OS in patients with TC tumours compared with lobectomy. However, most previous studies include not only both typical and atypical histological subtypes but also the whole range of stages from localized, regional to the distant stage.

In this population-based cohort, we evaluated the effect of surgical type on survival rates of stage T1-2N0M0 TC patients. Before matching, significant differences in clinical characteristics were seen between patients who received lobectomy or sublobar resection, which may affect the prognosis. Specifically, patients who underwent sublobar resection were more likely to be older and to have smaller tumours and had a lower proportion of LNs dissected. All baseline characteristics were well-balanced with PSM. After reducing potential confounding biases, we found that there was no significant difference in survival between patients with stage T1-2N0M0 TC tumours who received lobectomy and those who received sublobar resection. To our knowledge, this study is the first to compare the long-term oncological outcomes of sublobar resection and lobectomy for TC patients staged as T1-2N0M0 according to the 8th edition TNM staging system.

When analysed using the tumour size subgroup analysis, lobectomy conferred a similar OS compared with sublobar resection among each of the tumour size subgroups. This result was in line with previous studies. Brown *et al.* [16]. demonstrated that sublobar resection could achieve identical OS in 1495 resected patients with clinical stage T1aN0M0 TC tumours ≤2cm in size compared with lobectomy. Similarly, an analysis from the SEER programme [15] found that extent of resection was not associated with OS in early-stage TCs ≤2 cm in size, while there was poor survival for tumours with a diameter of $2\,\text{cm} < T \leq 3\,\text{cm}$ among patients who underwent sublobar resection. However, after further adjusting lymph node assessment using PSM, there was no significant survival difference between the 2 surgical approaches among all the subgroups stratified by tumour size.

As with early-stage NSCLC, lobectomy with thorough mediastinal lymph node dissection is currently recommended as the

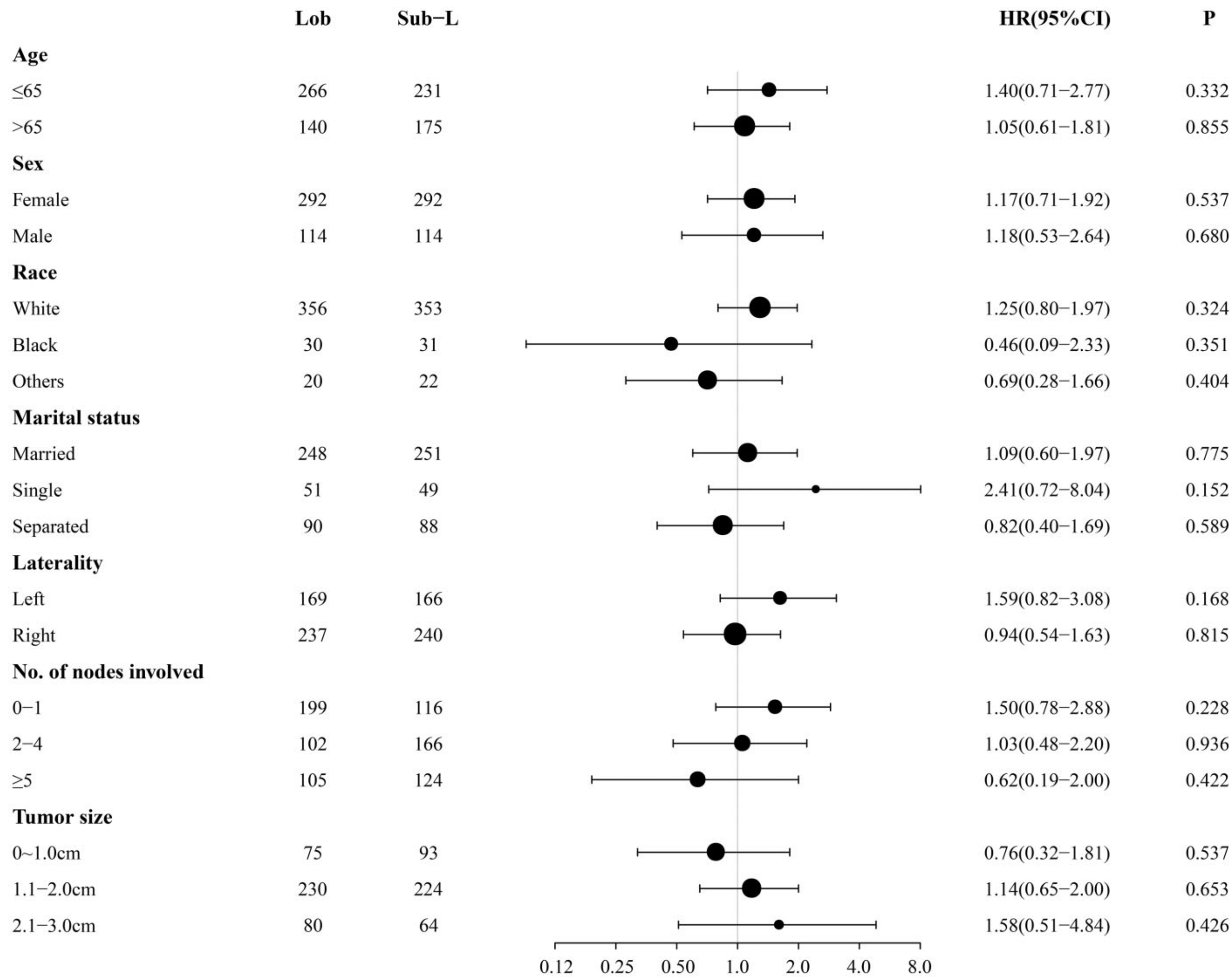


Figure 4: Subgroup analysis for overall survival in the matched population.

standard treatment for localized PCs. Sublobar resection, including anatomical segmentectomy and non-anatomical wedge resection, is recognized as a compromising procedure for high-risk patients [2, 11]. However, TCs usually have indolent growth and are generally associated with poorer invasion and a better prognosis compared with ACs. Lymph node-negative TC patients experienced relatively low risks of relapse and favourable outcomes [20]. And current National Comprehensive Cancer Network guidelines recommend observation after surgical therapy for patients with stage I to IIIA TC tumours [2]. All the abovementioned factors indicate that the contribution of the extent of surgery to prognosis was slight for early-stage TC tumours due to indolent biological properties. Cusumano *et al.* [21]. suggested that anatomical sublobar resection was advisable for small peripheral TCs. And our data demonstrate that sublobar resection was not inferior to lobectomy in patients with stage T1-2N0M0 TC tumours. Therefore, we support sublobar resection as a preferential surgical option for TC patients without lymph node or distant metastasis if lymph node assessment is performed adequately. Although some surgeons believe that TC tumours still have the tendency to distantly metastasize and more aggressive resection should be implemented due to the unpredictable development of the disease, the most important outcome is OS, and we did not observe survival differences in OS between patients undergoing lobectomy and those undergoing sublobar resection. More studies of perioperative outcome and disease recurrence rate comparing the potential difference between sublobar resection and lobectomy are required to provide further evidence.

In this study, we found that segmental resection and wedge resection had a similar prognosis, which was similar to the results of previous studies [15, 22]. Xu *et al.* [15]. reported that segmental resection conferred a similar OS to wedge resection in PCs. The study by Yan *et al.* [22]. showed that wedge resection was a comparable treatment to segmental resection for TC patients at the localized stage. However, patients who underwent wedge resection were more likely to be older and associated with a lower proportion of LNs dissected, which might affect the prognosis (seen in Supplementary Material, Table S1). Due to the lack of randomized controlled trials of TCs, the difference between the prognostic outcomes of segmentectomy and wedge resection needs further investigation in prospective studies.

In the multivariable analysis, the results of this study demonstrated that age, gender, marital status and lymph node

Table 2: Univariable and multivariable analyses for overall survival in the whole cohort

Characteristics	Univariable		Multivariable	
	HR (95% CI)	*P*-Value	HR (95% CI)	*P*-Value
Age (years)				
≤65	Reference		Reference	
≥66	3.58 (2.72–4.71)	<0.001	3.40 (2.55–4.44)	<0.001
Sex				
Female	Reference		Reference	
Male	0.78 (0.57–1.06)	0.116	1.49 (1.08–4.44)	0.014
Race				
White	Reference			
Black	0.98 (0.56–1.73)	0.958		
Others	0.83 (0.39–1.77)	0.635		
Marital status				
Married	Reference		Reference	
Single	1.19 (0.79–1.81)	0.406	1.52 (1.00–5.44)	0.051
Separated	2.16 (1.59–2.94)	<0.001	1.53 (1.12–5.44)	0.008
Unknown	1.13 (0.55–2.31)	0.745	1.00 (0.49–0.44)	0.994
Laterality				
Left	Reference			
Right	0.96 (0.73–1.27)	0.770		
Primary tumour site				
Upper lobe, lung	Reference			
Middle lobe, lung	1.02 (0.70–1.48)	0.924		
Lower lobe, lung	0.94 (0.69–1.29)	0.711		
Overlapping lesion of lung	1.42 (0.52–3.89)	0.497		
Lung, NOS	1.20 (0.60–2.40)	0.605		
Grade				
I	Reference			
II	0.70 (0.35–1.41)	0.320		
III/IV	0.92 (0.23–3.78)	0.913		
Unknown	1.03 (0.76–1.40)	0.834		
Number of nodes involved				
0–1	Reference		Reference	
2–4	0.66 (0.46–0.93)	0.017	0.70 (0.49–7.44)	0.043
≥5	0.48 (0.35–0.65)	<0.001	0.50 (0.37–5.44)	<0.001
Tumour size				
0–3.0 cm	Reference			
3.1–5.0 cm	0.88 (0.58–1.35)	0.555		
Radiotherapy				
No	Reference			
Yes	1.19 (0.30–4.79)	0.808		
Adjuvant chemotherapy				
No	Reference		Reference	
Yes	2.70 (1.11–6.56)	0.028	2.01 (0.82–0.44)	0.127
Surgery				
Lobectomy	Reference		Reference	
Sublobar resection	1.83 (1.39–2.42)	<0.001	1.17 (0.83–1.44)	0.369

CI: confidence interval; HR: hazard ratio; NOS: not otherwise specified.

assessment remained the independent prognostic factors associated with OS, whereas the extent of resection was not. Age ≤65 years, female sex, married status and adequate lymph node assessment (≥5) were associated with improved OS. Our results were highly consistent with previous results [15]. Previous research found that patients who were older at onset had more comorbidities, poorer performance status, lower tolerance of treatment and a worse prognosis [23, 24]. Some studies have reported a worse prognosis in females than males [25, 26]. Differences in constitutional, physiological and social factors may explain this survival discrepancy. Specific mechanisms may require further research. Previous studies [27, 28] showed that all unmarried individuals (single, divorced and widowed) developed more anxiety symptoms and had a worse prognosis than the married group, indicating that unmarried status may be relevant to complex social physiology levels. Further studies are necessary to elucidate the specific mechanism. Lymph node dissection is the focus of surgery, and the appropriate extent of lymph node dissection to obtain better survival has been the focus of clinical research. Our study demonstrated that detecting 5 or more lymph nodes yielded good long-term survival benefits for stage T1-2N0M0 TC patients. A large population-based study [29] proposed that the detection of ≥16 lymph nodes can improve the accuracy of node staging and the long-term survival of resected NSCLC. A study based on the National Cancer Database [30] found that patients may benefit from retrieval of ≥7 lymph nodes during lobectomy for limited-stage small-cell lung cancer, but the optimal number of lymph nodes that should be removed for TC tumours remains unclear.

Limitations

The study had some limitations. First, potential selection bias is inevitable in retrospective studies. Unmeasured confounders or missing data might introduce bias into the results. Despite the use of PSM, there are still unadjusted confounding variables. Smoking history, performance status, comorbidities, complications, pulmonary function testing results, details on patient selection, clinical follow-up, heterogeneity in surgical management, surgical margin status and tumour location (central versus peripheral) are not available in the SEER database, which may result in bias in these research results. Second, detailed therapeutic options regarding radiotherapy, chemotherapy regimens, targeted therapy records and endocrine therapy are not available. Third, it is difficult to assess lymph node status when patients underwent wedge resection. A small proportion of N1 patients receive wedge resection, which would undoubtedly add to the number of surgical candidates, perhaps resulting in bias in the research results. Fourth, because the number in the $T > 3$ cm group was low, statistical analysis was not applied for separate subgroup analysis. The prognostic difference between the sublobar resection group and the lobectomy group is difficult to discern in this tumour size subgroup. Fifth, in clinical practice central type TCs were not indicative for wedge resection, and TCs originating from lobar bronchus were not managed with segmentectomy; this bias on selecting operation mode persists despite the use of PSM. Sixth, the number of LNs examined was identified as an independent prognostic factor. Before matching, the number of LNs examined for the sublobar resection group was only 2.30, whereas for the lobectomy group it was 7.98. After matching, the number of LNs examined for the sublobar resection group was 3.57, and for the lobectomy group, it was 3.84, which inadvertently selected the most aggressive nodal dissection cases from the sublobar resection group and the least nodal dissections from the lobectomy group. This may affect interpretation of the results. Finally, the number of events (death) was very small in both the lobectomy group and the sublobar resection group, and the results of multivariable analyses are unstable, which may result in bias in this research results. Therefore, the interpretation of these results is limited.

CONCLUSION

In conclusion, according to the results of our SEER database analysis and the PSM analysis, sublobar resection is not inferior to lobectomy for stage T1-2N0M0 TC tumours. Considering sublobar resection better preserves lung function and decreases postoperative complications, sublobar resection may be a reasonable treatment option for patients with TC tumours ≤ 5 cm in size without lymph node or distant metastasis if lymph node assessment is performed adequately. Further randomized controlled studies should be performed to confirm these findings.

SUPPLEMENTARY MATERIAL

Supplementary material is available at *ICVTS* online.

ETHICAL APPROVAL

This article does not contain any studies with human participants or animals performed by any of the authors.

INFORMED CONSENT

Informed consent is waived as SEER, which is a de-identifed, publicly available cancer database.

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Data Availability Statement

All data included in this study are available upon request by contact with the corresponding author.

Author contributions

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REFERENCES

[1] Prinzi N, Rossi RE, Proto C, Leuzzi G, Raimondi A, Torchio M *et al.* Recent advances in the management of typical and atypical lung carcinoids. Clin Lung Cancer 2021;22:161–9.

[2] Baudin E, Caplin M, Garcia-Carbonero R, Fazio N, Ferolla P, Filosso PL *et al.*; ESMO Guidelines Committee. Lung and thymic carcinoids: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 2021;32:439–51.

[3] Chiappetta M, Sperduti I, Ciavarella LP, Leuzzi G, Bria E, Mucilli F *et al.* Prognostic score for survival with pulmonary carcinoids: the importance of associating clinical with pathological characteristics. Interact CardioVasc Thorac Surg 2020;31:315–23.

[4] Yao JC, Hassan M, Phan A, Dagohoy C, Leary C, Mares JE *et al.* One hundred years after "carcinoid": epidemiology of and prognostic factors for neuroendocrine tumors in 35,825 cases in the United States. JCO 2008; 26:3063–72.

[5] Furqan M, Tien YY, Schroeder MC, Parekh KR, Keech J, Allen BG *et al.* Lobar versus sub-lobar surgery for pulmonary typical carcinoid, a population-based analysis. J Thorac Dis 2018;10:5850–9.

[6] Kneuertz PJ, Kamel MK, Stiles BM, Lee BE, Rahouma M, Harrison SW *et al.* Incidence and prognostic significance of carcinoid lymph node metastases. Ann Thorac Surg 2018;106:981–8.

[7] Rea F, Rizzardi G, Zuin A, Marulli G, Nicotra S, Bulf R *et al.* Outcome and surgical strategy in bronchial carcinoid tumors: single institution experience with 252 patients. Eur J Cardiothorac Surg 2007;31:186–91.

[8] Gosain R, Groman A, Yendamuri SS, Iyer R, Mukherjee S. Role of adjuvant chemotherapy in pulmonary carcinoids: an NCDB analysis. Anticancer Res 2019;39:6835–42.

[9] Nussbaum DP, Speicher PJ, Gulack BC, Hartwig MG, Onaitis MW, D'Amico TA *et al.* Defining the role of adjuvant chemotherapy after lobectomy for typical bronchopulmonary carcinoid tumors. Ann Thorac Surg 2015;99:428–34.

[10] Gosain R, Mukherjee S, Yendamuri SS, Iyer R. Management of typical and atypical pulmonary carcinoids based on different established guidelines. Cancers 2018;10:510.

[11] Gu C, Wang R, Pan X, Huang Q, Zhang Y, Yang J *et al.* Sublobar resection versus lobectomy in patients aged ≤ 35 years with stage IA non-small cell lung cancer: a SEER database analysis. J Cancer Res Clin Oncol 2017;143: 2375–82.

[12] Zhang B, Liu R, Ren D, Li X, Wang Y, Huo H *et al.* Comparison of lobectomy and sublobar resection for stage IA elderly NSCLC patients (≥70 years): a population-based propensity score matching's study. Front Oncol 2021;11:610638.

[13] von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP; STROBE Initiative. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. Epidemiology 2007;18:800–4.

[14] Shah S, Gosain R, Groman A, Gosain R, Dasari A, Halfdanarson TR *et al.* Incidence and survival outcomes in patients with lung neuroendocrine neoplasms in the United States. Cancers (Basel) 2021;13:1753.

[15] Xu S, Li X, Ren F, He J, Zhao S, Wang Y *et al.* Sublobar resection versus lobectomy for early-stage pulmonary carcinoid tumors ≤3 cm in size: a SEER population-based study. Ann Surg 2020. https://doi.org/10.1097/SLA.0000000000004593.

[16] Brown LM, Cooke DT, Jett JR, David EA. Extent of resection and lymph node assessment for clinical stage T1aN0M0 typical carcinoid tumors. Ann Thorac Surg 2018;105:207–13.

[17] Fox M, Van Berkel V, Bousamra M 2nd, Sloan S, Martin RC 2nd. Surgical management of pulmonary carcinoid tumors: sublobar resection versus lobectomy. Am J Surg 2013;205:200–8.

[18] Yendamuri S, Gold D, Jayaprakash V, Dexter E, Nwogu C, Demmy T. Is sublobar resection sufficient for carcinoid tumors. Ann Thorac Surg 2011;92:1774–8, discussion 1778–9.

[19] Raz DJ, Nelson RA, Grannis FW, Kim JY. Natural history of typical pulmonary carcinoid tumors: a comparison of nonsurgical and surgical treatment. Chest 2015;147:1111–7.

[20] Lou F, Sarkaria I, Pietanza C, Travis W, Roh MS, Sica G *et al.* Recurrence of pulmonary carcinoid tumors after resection: implications for postoperative surveillance. Ann Thorac Surg 2013;96:1156–62.

[21] Cusumano G, Fournel L, Strano S, Damotte D, Charpentier MC, Galia A *et al.* Surgical resection for pulmonary carcinoid: long-term results of multicentric study—the importance of pathological N status, more than we thought. Lung 2017;195:789–98.

[22] Yan T, Wang K, Liu J, Zeng Y, Bie F, Wang G *et al.* Wedge resection is equal to segmental resection for pulmonary typical carcinoid patients at localized stage: a population-based analysis. PeerJ 2019;7:e7519.

[23] Pilleron S, Maringe C, Charvat H, Atkinson J, Morris E, Sarfati D. Age disparities in lung cancer survival in New Zealand: the role of patient and clinical factors. Lung Cancer 2021;157:92–9.

[24] Ahmed T, Lycan T, Dothard A, Ehrlichman P, Ruiz J, Farris M *et al.* Performance Status and age as predictors of immunotherapy outcomes in advanced non-small-cell lung cancer. Clin Lung Cancer 2020;21:e286–286e293.

[25] Dong S, Liang J, Zhai W, Yu Z. Development and validation of an individualized nomogram for predicting overall survival in patients with typical lung carcinoid tumors. Am J Clin Oncol 2020;43:607–14.

[26] Huang Y, Yang X, Lu T, Li M, Zhao M, Yang X *et al.* Assessment of the prognostic factors in patients with pulmonary carcinoid tumor: a population-based study. Cancer Med 2018;7:2434–41.

[27] Xie JC, Yang S, Liu XY, Zhao YX. Effect of marital status on survival in glioblastoma multiforme by demographics, education, economic factors, and insurance status. Cancer Med 2018;7:3722–42.

[28] Chen Z, Yin K, Zheng D, Gu J, Luo J, Wang S *et al.* Marital status independently predicts non-small cell lung cancer survival: a propensity-adjusted SEER database analysis. J Cancer Res Clin Oncol 2020;146:67–74.

[29] Liang W, He J, Shen Y, Shen J, He Q, Zhang J *et al.* Impact of examined lymph node count on precise staging and long-term survival of resected non-small-cell lung cancer: a population study of the US SEER Database and a Chinese Multi-Institutional Registry. JCO 2017;35:1162–70.

[30] Rucker AJ, Raman V, Jawitz OK, Voigt SL, Tong BC, D'Amico TA *et al.* Effect of lymph node assessment on outcomes in surgery for limited stage small cell lung cancer. Ann Thorac Surg 2020;110:1854–60.