Original Article

The association of postoperative radiotherapy with survival in resected N2 non-small cell lung cancer

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Background: The current staging system for completely resected pathologic N2 non-small cell lung cancer (NSCLC) treated with chemotherapy is not suitable for distinguishing those patients most likely to benefit from postoperative radiotherapy (PORT). This study aimed to construct a survival prediction model that will enable individualized prediction of the net survival benefit of PORT in patients with completely resected N2 NSCLC treated with chemotherapy.

Methods: A total of 3,094 cases from between 2002 and 2014 were extracted from the Surveillance, Epidemiology, and End Results (SEER) database. Patient characteristics were included as covariates, and their association with overall survival (OS) with and without PORT was assessed. Data from 602 patients from China were included for external validation.

Results: Age, sex, the number of examined/positive lymph nodes, tumor size, the extent of surgery, and visceral pleural invasion (VPI) were significantly associated with OS ($P<0.05$). Two nomograms were developed based on clinical variables to estimate individuals' net survival difference attributable to PORT. The calibration curve showed excellent agreement between the OS predicted by the prediction model and that actually observed. In the training cohort, the C-index for OS was 0.619 [95% confidence interval (CI): 0.598–0.641] in the PORT group and 0.627 (95% CI: 0.605–0.648) in the non-PORT group. Results showed that PORT could improve OS [hazard ratio (HR): 0.861; $P=0.044$] for patients with a positive PORT net survival difference.

Conclusions: Our practical survival prediction model can be used to make an individualized estimate of the net survival benefit of PORT for patients with completely resected N2 NSCLC who have been treated with chemotherapy.

Keywords: Postoperative radiotherapy (PORT); pathologic N2 non-small cell lung cancer; nomogram

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Introduction

Lung cancer is responsible for 18.4% of all cancer deaths, making it the leading cause of cancer-associated mortality worldwide (1). Patients with resected pathologic N2 non-small cell lung cancer (NSCLC) are a high-risk group for regional recurrence and metastasis, even with complete resection (2). The National Comprehensive Cancer Network (NCCN) guidelines currently recommend adjuvant chemotherapy for patients who undergo resection for pathologic N2 NSCLC (3); however, there a lack of consensus regarding the benefit of postoperative radiotherapy (PORT) for this group.

Data from two large databases, Surveillance, Epidemiology, and End Results (SEER) (4) and National Cancer Database (NCDB) (5), suggest that PORT can improve survival for patients with resected pathologic N2 NSCLC. Meta-analyses have also revealed a benefit of PORT in N2 nodal disease (6,7). Further, the subgroup investigation of the Lung ART trial verified that PORT could decrease the local recurrence rate for these patients. However, other studies have suggested that PORT has no significant effect on survival (8-12), and the NCCN guidelines do not give a clear recommendation on whether PORT is required (3). Therefore, the role of PORT in the treatment of completely resected N2 NSCLC is still highly controversial.

In addition to the lack of evidence to suggest that PORT can be beneficial to patients, the current staging system for completely resected pathologic N2 NSCLC treated with chemotherapy is not sufficient for identifying those patients who are most likely to benefit from PORT. Therefore, developing a survival model exploring the potential individual benefit of PORT remains necessary.

In this study, we aimed to develop a survival prediction model to calculate the probable overall survival (OS) differences with or without PORT in patients with completely resected pathologic N2 NSCLC treated with chemotherapy. We present the following article in accordance with the TRIPOD reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-22-772/rc).

Methods

Patient selection

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The Ethics Committee of the First Affiliated Hospital of Guangzhou Medical University approved this study (approval No. 2020 No. 69; issue date: 13/3/2020). Individual consent for this retrospective analysis was waived.

Information of patients with completely resected pathologic N2 NSCLC treated with chemotherapy from between 2002 and 2014 was extracted from the SEER database (http://seer.cancer.gov/). Patients were included if they: had pathologically confirmed primary N2 NSCLC between January 2002 and December 2014, had a history of complete resection through lobectomy or pneumonectomy, had received treatment with chemotherapy, and had only one malignant primary lesion. Patients were excluded if they: had distant metastasis; had invasion of the heart, great vessels, trachea, diaphragm, mediastinum, recurrent laryngeal nerve, carina, vertebral body, or esophagus; had undergone preoperative radiotherapy; had radioactive implants; had received radioisotopes; or had information missing from their extracted data.

An external validation cohort that met the same inclusion and exclusion criteria was included to analyze the applicability of the prediction model. The cohort consisted of 602 patients treated between 2009 and 2014 in the First Affiliated Hospital of Guangzhou Medical University and the Collaborative Innovation Center for Cancer Medicine of Sun Yat-sen University, China.

Baseline data of the demographics of the patients (age, sex, and race), tumor characteristics (size, location, differentiation grade, and histological type), the number of examined lymph nodes, the number of positive lymph nodes, the extent of surgery, and visceral pleural invasion (VPI) were gathered from the SEER database. The TNM categories were based on the International Association for the Study of Lung Cancer (IASLC) eighth edition staging system (13). Cases were categorized as having received or not received PORT (the PORT group and non-PORT group, respectively).

Construction of the nomogram

In the training set for the PORT and non-PORT groups, OS was predicted with the Kaplan–Meier method and analyzed by applying the log-rank test. Multivariable Cox proportional hazards regression was applied to identify independent prognostic factors. On the basis of the significant independent factors in the two groups, nomograms were formulated using R version 3.5.3 (R Core Team, Vienna, Austria) with the rms and survival

packages (14). The rms package corresponds with the book Regression Modeling Strategies. All survival models were constructed using the rms R library by Harrell (http://cran.r-project.org/web/packages/rms).

Validation and calibration of the nomogram

The model was subjected to 1,000 bootstrap resamples for internal validation in the training cohort and external validation in the cohort from the Chinese Institute. Calibration for 1-, 3-, and 5-year OS was determined by comparing the predicted survival with that observed on 1,000 bootstrap resamples. The discrimination ability of the model was determined using the concordance index (C-index). C-index values range from 0.5 to 1.0, with a higher value suggesting a better predictive performance (15). The C-index values for the two different models were compared using methods previously described (16).

Statistical analysis

The chi-square test was applied to examine the statistical significance of the differences in clinical variables between the PORT and non-PORT groups. OS was calculated using the Kaplan–Meier method and compared by applying the log-rank test. Independent prognostic factors were identified using multivariate Cox proportional hazards regression, and the hazard ratios (HRs) and corresponding 95% confidence intervals (CIs) were determined. The nomograms were developed using the rms package of R version 3.5.3 (R Core Team, Vienna, Austria). All statistical analyses were performed using SPSS 22.0 (IBM Corp, Armonk, NY, USA), and a P value less than 0.05 was regarded as statistically significant.

Results

Clinical characteristics

A total of 3,094 patients with completely resected pathologic N2 NSCLC who were treated with chemotherapy derived from the SEER database (Figure S1), and 602 patients from a multicenter hospital in China, met the inclusion criteria. The demographics and clinicopathological characteristics of patients in the training and external validation cohorts are listed in *Table 1*. The median interquartile range and follow-up times on OS were 27 months [13, 52] and 36 months [22, 49] in the training cohort and external validation cohort, respectively.

Independent prognostic factors in the training cohort

Survival analysis using the log-rank test found no significant differences in OS (HR =1.006; 95% CI: 0.915–1.106; P=0.9) between the PORT and non-PORT groups (*Figure 1*). Results from the multivariate regression model are listed in *Table 2*. For patients with PORT, the multivariate analysis indicated that age (P<0.001), sex (P=0.011), number of examined lymph nodes (P<0.001), number of positive lymph nodes (P<0.001), tumor size (P=0.037), extent of surgery (P=0.032), and differentiation grade (P=0.001) were independent prognostic factors for OS. For patients in the non-PORT group, the multivariate analysis indicated that age (P<0.001), sex (P<0.001), examined lymph nodes (P=0.013), the number of positive lymph nodes (P<0.001), tumor size (P=0.005), and VPI (P=0.046) were independent prognostic factors for OS.

Development of the prognostic nomogram

Nomograms were constructed from the coefficients from the multivariate regression model. Significant independent factors in the two groups, including age, sex, the number of examined lymph nodes, the number of positive lymph nodes, tumor size, the extent of surgery, differentiation grade, and VPI, were included to develop the nomograms. The first nomogram (*Figure 2A*) estimated OS with PORT, and the second nomogram (*Figure 2B*) estimated OS without PORT.

To estimate the net survival benefit of PORT, the two nomograms were used together (*Figure 2*). The difference between the two estimates represented the expected net survival benefit from the addition of PORT. Each factor was given a score on the point scale. By calculating the total score, finding it on the total point scale, and drawing a straight line, the estimated probability of survival at each score point could be easily determined.

Calibration and validation of the nomogram

In the training cohort, the calibration curves (*Figure 3A*,*3B*) showed strong agreement between the 1-, 3-, and 5-year OS predicted by the nomogram and that actually observed. In the PORT group, the value of Harrell's C-index for the nomogram established to predict OS (0.619; 95% CI: 0.598–0.641) was significantly greater than that of the IASLC eighth edition staging system (T1, T2, T3, and T4, 0.566; 95% CI: 0.521–0.610; P<0.01). In the non-PORT group, the C-index was higher for the nomogram

Table 1 Demographics and clinicopathologic characteristics of the training and external validation cohorts

Characteristic	Training cohort					External validation cohort				
	PORT (n=1,519)		No PORT (n=1,575)		P	PORT (n=69)		No PORT (n=533)		P
	No.	%	No.	%		No.	%	No.	%	
Age, years					0.001					0.127
<60	517	34	495	31.4		47	68.1	295	55.3	
60–70	594	39.1	558	35.4		17	24.6	177	33.2	
≥70	408	26.9	522	33.1		5	7.2	61	11.4	
Sex					0.272					0.25
Male	734	48.3	730	46.3		45	65.2	309	58	
Female	785	51.7	845	53.7		24	34.8	224	42	
Race					0.674					
White	1,236	81.4	1,285	81.6		–	–	–	–	
Black	138	9.1	152	9.7		–	–	–	–	
Other	145	9.5	138	8.8		–	–	–	–	
Location					0.732					0.856
Upper	875	57.6	896	56.9		31	44.9	258	48.4	
Middle	75	4.9	72	4.6		7	10.1	41	7.7	
Lower	516	34	548	34.8		28	40.6	206	38.6	
Other	53	3.3	59	3.7		3	4.3	28	5.3	
Examined lymph nodes					0.035					0.837
0–9	696	45.8	649	41.2		7	10.1	46	8.6	
10–15	404	26.6	453	28.8		13	18.8	114	21.4	
≥16	419	27.6	473	30		49	71	373	70	
Positive lymph nodes					0.007					0.963
1–3	876	57.7	995	63.2		26	37.7	210	39.4	
4–9	531	35	478	30.3		28	40.6	211	39.6	
≥10	112	7.4	102	6.5		15	21.7	112	21	
Tumor size, cm										
≤3	715	47.1	719	45.7	0.305	30	43.5	259	48.6	0.524
>3 to 5	522	34.4	525	33.3		29	42	183	34.3	
>5 to 7	187	12.3	230	14.6		5	7.2	58	10.9	
>7	95	6.3	101	6.4		5	7.2	33	6.2	
Extent of surgery					0.01					0.3
Lobectomy	1,385·	91.2	1,392	88.4		68	98.6	512	96.1	
Pneumonectomy	134	8.8	183	11.6		1	1.4	21	3.9	

Table 1 (*continued*)

Table 1 (*continued*)

Characteristic	Training cohort					External validation cohort				
	PORT (n=1,519)		No PORT (n=1,575)		P	PORT (n=69)		No PORT (n=533)		P
	No.	%	No.	%		No.	%	No.	%	
Differentiation grade					0.834					0.126
Grade I	72	4.7	83	5.3		1	1.4	17	3.2	
Grade II	633	41.7	663	42.1		33	47.8	289	54.2	
Grade III or IV	713	46.9	733	46.5		19	27.5	158	29.6	
Unknown	101	6.6	96	6.1		16	23.2	69	12.9	
Histology					0.71					0.007
SC	273	18	305	19.4		23	33.3	93	17.4	
Adenocarcinoma	1,028	67.7	1,038	65.9		42	60.9	405	76	
Others	218	14.4	232	14.7		4	5.8	35	6.6	
VPI					0.195					0.968
Yes	537	35.4	522	33.1		34	49.3	264	49.5	
No	982	64.6	1,053	66.9		35	50.7	269	50.5	

PORT, postoperative radiotherapy; SC, squamous carcinoma; VPI, visceral pleural invasion.

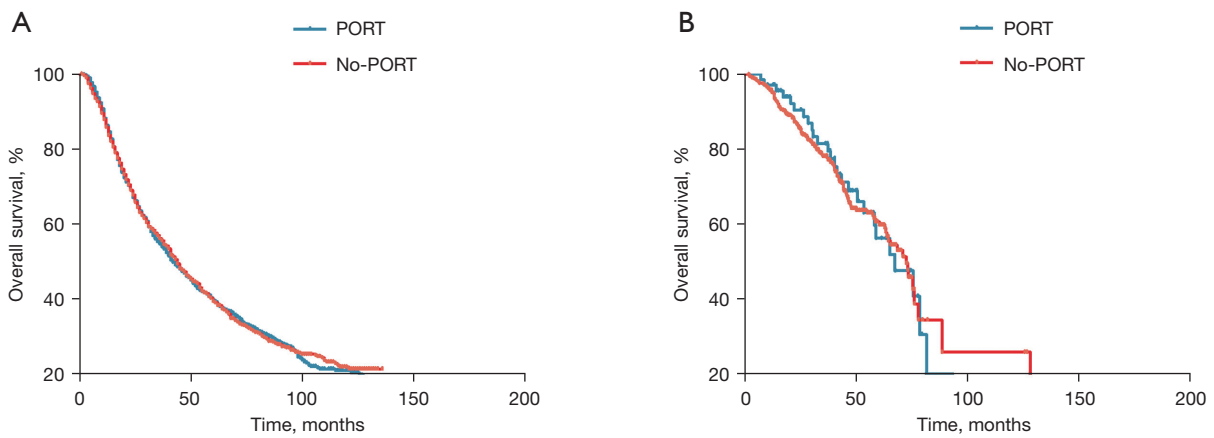

Figure 1 Kaplan-Meier estimates of OS for patients with completely resected pathologic N2 NSCLC treated with chemotherapy. (A) The estimated OS for patients in the training cohorts. (B) The estimated OS for patients in the external validation cohorts. PORT, postoperative radiotherapy; OS, overall survival; NSCLC, non-small cell lung cancer.

0.627 (95% CI: 0.605–0.648) than it was for the T category prediction (0.559; 95% CI: 0.540–0.610; P<0.01). In the external validation cohort, the calibration plots also presented acceptable agreement between the nomogram predictions and actual observations for 1-, 3-, and 5-year OS (*Figure 3C,3D*). The C-index was 0.599 (95% CI: 0.485–0.713) for the PORT group and 0.595 (95% CI: 0.544–0.646) for the non-PORT group.

Clinical use

For each individual patient, we used nomogram A to

Table 2 Multivariate Cox regression analysis of factors associated with overall survival

Characteristic	PORT (n=1,519)				No PORT (n=1,575)			
	Univariable analysis, P value	Multivariable analysis			Univariable analysis, P value	Multivariable analysis		
		Hazard ratio	95% CI	P value		Hazard ratio	95% CI	P value
Age, years	<0.001			<0.001	<0.001			<0.001
<60		1 (reference)				1 (reference)		
60–70		1.203	1.019 to 1.419	0.029		1.100	0.927 to 1.306	0.274
≥70		1.531	1.283 to1.828	<0.001		1.642	1.387 to 1.944	<0.001
Sex	0.003				<0.001			
Male		1 (reference)				1 (reference)		
Female		0.835	0.727 to 0.959	0.011		0.702	0.613 to 0.803	<0.001
Race	0.238				0.011			0.107
White		–	–	–		1 (reference)		
Black		–	–	–		0.983	0.779 to 1.242	0.981
Other		–	–	–		0.759	0.587 to 0.980	0.034
Location	0.046			0.301	0.069			0.814
Upper		1 (reference)				1 (reference)		
Middle		0.982	0.694 to 1.388	0.916		1.040	0.74 to 1.461	0.82
Lower		1.034	0.889 to 1.203	0.663		1.073	0.928 to 1.242	0.34
Other		0.650	0.313 to 1.350	0.248		0.995	0.692 to 1.432	0.98
Examined lymph nodes	0.075			<0.001	0.435			0.013
0–9		1 (reference)				1 (reference)		
10–15		0.792	0.666 to 0.942	0.008		0.842	0.714 to 0.993	0.041
≥16		0.660	0.546 to 0.797	<0.001		0.775	0.649 to 0.927	0.005
Positive lymph nodes	<0.001			<0.001	<0.001			<0.001
1–3		1 (reference)				1 (reference)		
4–9		1.423	1.218 to 1.662	<0.001		1.345	1.155 to 1.568	<0.001
≥10		1.849	1.397 to 2.448	<0.001		1.841	1.400 to 2.423	<0.001
Tumor size, cm	<0.001			0.037	<0.001			0.005
≤3		1 (reference)				1 (reference)		
>3 to 5		1.145	0.978 to 1.340	0.92		1.150	0.984 to 1.345	0.08
>5 to 7		1.341	1.083 to 1.660	0.007		1.241	1.007 to 1.528	0.042
≥7		1.245	0.934 to 1.661	0.135		1.605	1.221 to 2.109	0.001
Extent of surgery	0.007				0.016			
Lobectomy		1 (reference)				1 (reference)		
Pneumonectomy		1.308	1.024 to 1.671	0.032		1.117	0.896 to 1.391	0.326

Table 2 (*continued*)

Table 2 (*continued*)

Characteristic	PORT (n=1,519)				No PORT (n=1,575)			
	Univariable analysis, P value	Multivariable analysis			Univariable analysis, P value	Multivariable analysis		
		Hazard ratio	95% CI	P value		Hazard ratio	95% CI	P value
Differentiation grade	0.011			0.001	0.142			0.317
Grade I		1 (reference)				1 (reference)		
Grade II		1.338	0.895 to 2.000	0.156		1.254	0.906 to 1.735	0.173
Grade III or IV		1.721	1.154 to 2.565	0.008		1.335	0.966 to 1.846	0.08
Unknown		1.639	1.010 to 2.660	0.045		1.365	0.903 to 2.063	0.14
Histology	0.374	–	–	–	0.825	–	–	–
SC		–	–	–		–	–	–
Adenocarcinoma		–	–	–		–	–	–
Others		–	–	–		–	–	–
VPI	0.029				0.012			
Yes		1 (reference)				1 (reference)		
No		1.146	0.991 to 1.326	0.66		1.157	1.003 to 1.335	0.046

PORT, postoperative radiotherapy; CI, confidence interval; SC, squamous carcinoma; VPI, visceral pleural invasion.

first calculate the expected OS with PORT, then we used nomogram B to calculate the expected OS without PORT. The difference between the two estimates represented the expected net survival difference from the addition of PORT. The net survival difference was computed for each patient based on their 3-year survival rates calculated using the two nomograms.

In the SEER dataset, there were 1,434 patients with a positive PORT net survival difference and 1,475 patients with a negative PORT net survival difference. The multivariate analyses showed that PORT could improve OS (HR: 0.861; 95% CI: 0.744–0.996; P=0.044) for patients with a positive PORT net survival difference. However, for patients with a negative PORT net survival difference, PORT was not significantly associated with OS (HR: 1.113; 95% CI: 0.978–1.267; P=0.105). The Kaplan–Meier curves for OS are shown in Figure S2.

Discussion

We established a practical survival prediction model that can be used to make individualized predictions about the expected survival benefit of PORT for patients with completely resected pathologic N2 NSCLC treated with chemotherapy. For the patients in our analysis, the model had a better predictive performance than the T category of the IASLC eighth edition staging manual, as indicated by its higher C-index. Our model is practical for individualized recommendations for the use of PORT.

Adjuvant chemotherapy is recommended for patients with completely resected pathologic N2 by the NCCN guidelines (3). Therefore, our study excluded patients who had not undergone chemotherapy. In this large population-based study, our results revealed no statistical differences in OS between the PORT and non-PORT groups (*Figure 1*). Consistent with this result, an early closed randomized controlled trial indicated that PORT increased both the local/regional and distant disease-free survival rates but not the OS rate (9). A randomized phase III study (8) with 37 patients and a phase II trial with 101 patients (10) also showed that there were no statistical differences in OS between the observation and PORT arms. Further, a randomized controlled trial (Lung-Art Trial, NCT00410683) of the ESMO (European Society for Medical Oncology) congress and the most recent phase III clinical trial (12) results showed that PORT had no progression-free survival PFS or OS benefit for patients with R0 resection N2 (IIIA) of NSCLC. Both studies mentioned

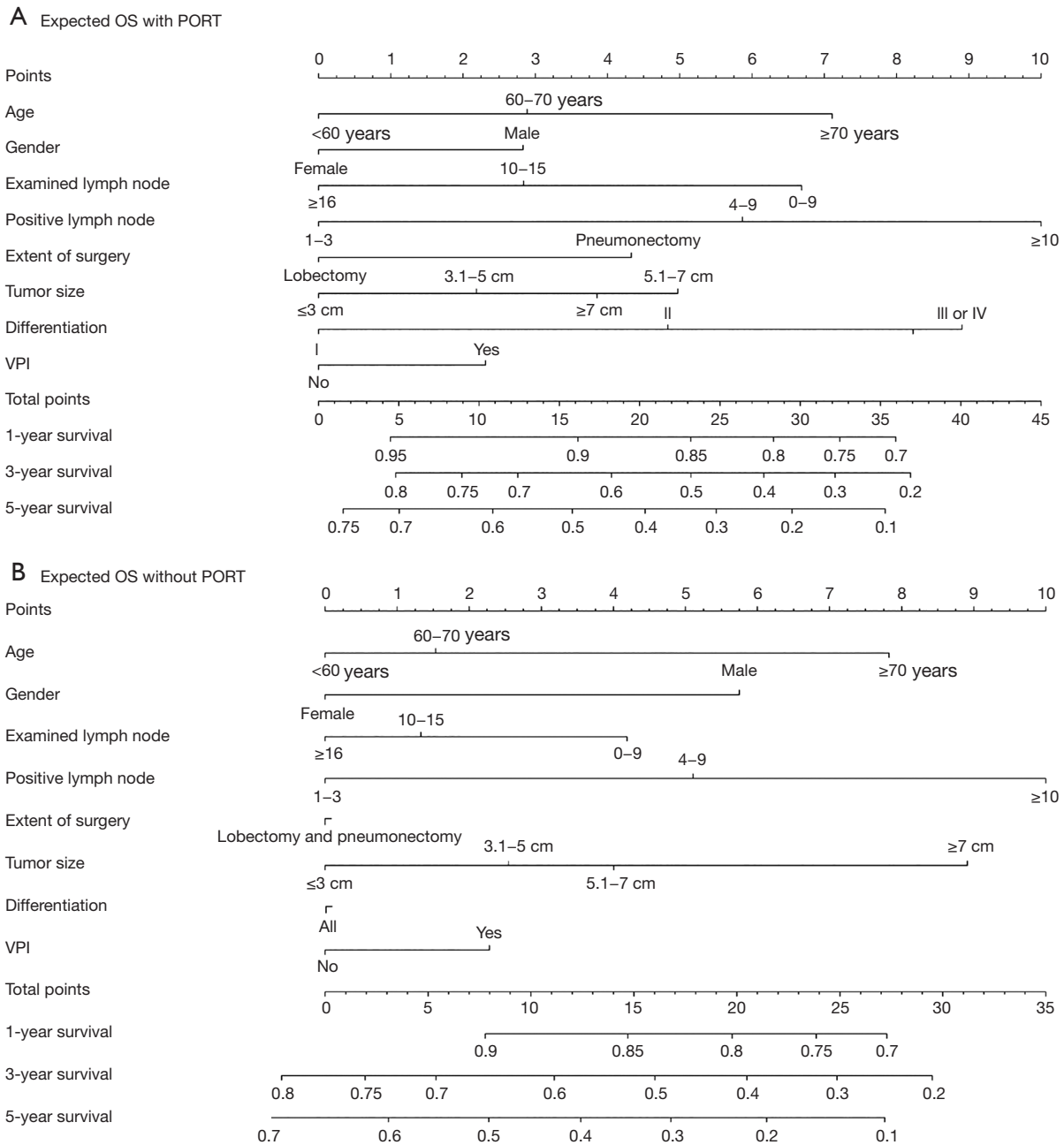

Figure 2 Nomograms comparing the expected OS with and without PORT. For each individual patient, we first used nomogram (A) to calculate the expected OS with PORT; then, we used nomogram (B) to calculate the expected OS without PORT. The difference between the two estimates represents the expected net survival impact with PORT and without PORT. OS, overall survival; PORT, postoperative radiotherapy; VPI, visceral pleural invasion.

prognostic models considering disease-free survival but suggested that further studies were needed to investigate the benefit of PORT for patients. Our study based on a large cohort from the SEER database obtained the same result for OS. However, previous retrospective studies and meta-analyses found that PORT could significantly improve the survival of patients (4-7). Therefore, the benefit of PORT for patients with completely resected N2

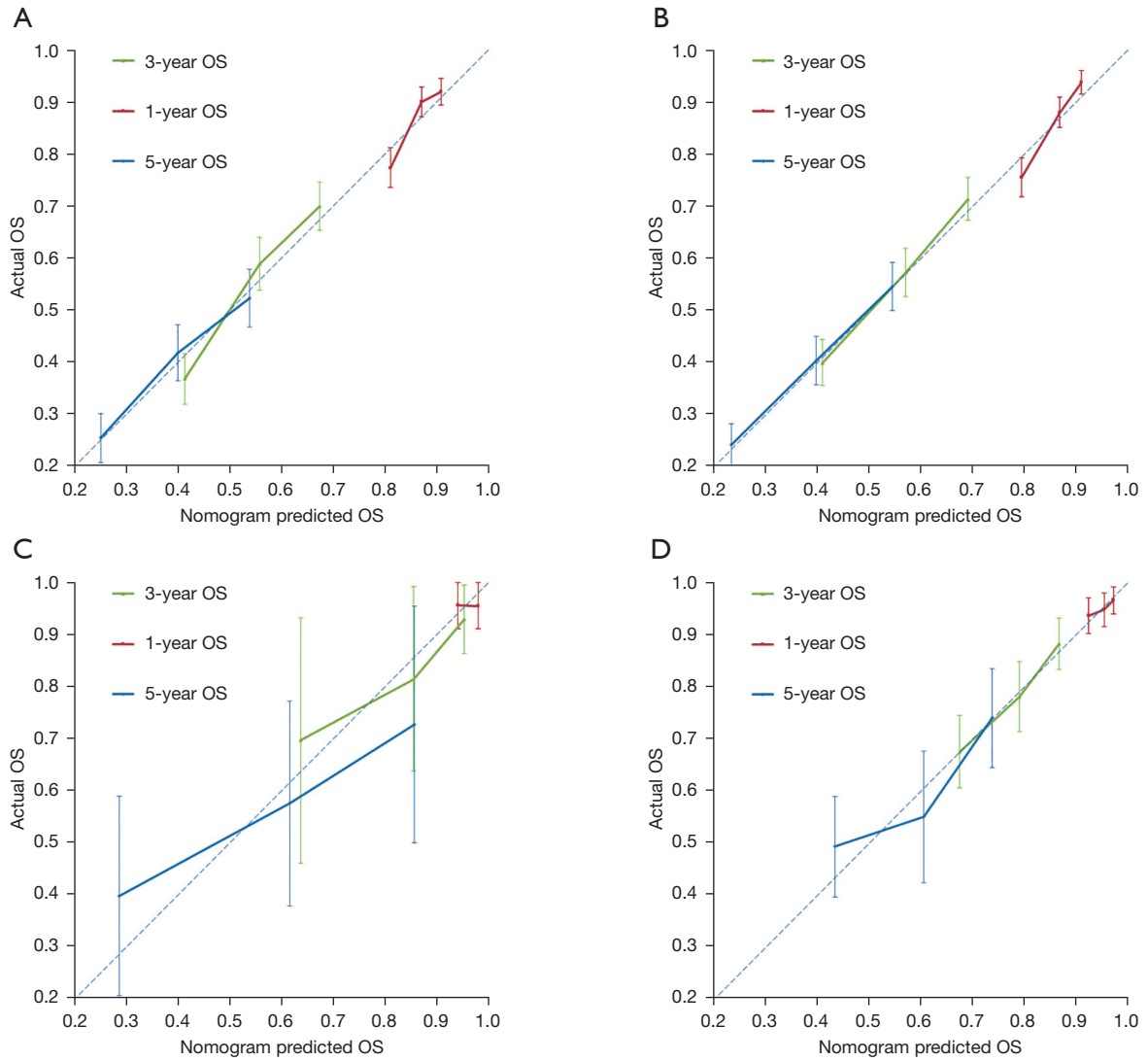

Figure 3 Calibration of the nomograms in the training and external validation cohorts. The X-axis represents nomogram-predicted survival and the Y-axis represents actual survival; the 95% CIs were measured using Kaplan-Meier analysis. Calibration curves of the PORT (A) and non-PORT (B) groups in the training cohort. Calibration curves of the PORT (C) and non-PORT (D) groups in the external validation cohort. OS, overall survival; PORT, postoperative radiotherapy.

is still controversial. Our nomograms may also be valuable for identifying those patients most likely to benefit from PORT; using the nomograms, we found that approximately half of the patients in our study might have benefited from PORT (Figure S2).

It is unclear why the results of our study differ from those of others (4,5). A possible explanation is the difference in the prognostic factors included in the multivariate analyses. For example, the numbers of positive lymph nodes and examined lymph nodes were not reported in previous NCDB studies (5,17). However, the number of positive lymph nodes is an essential prognostic factor in many cancers, and comparable studies have suggested that a higher number of positive lymph nodes (n>3) is associated with a poorer survival rate (18,19). Further, examined lymph node count is also an important prognostic factor for NSCLC (20). The independent prognostic factors of age, sex, tumor size, and extent of surgery in our study were also identified in some prior studies for NSCLC (5,21,22). Our study did not select histology as a candidate factor because

it was not an independent prognostic factor. This finding is consistent with those of other studies on stage II or III (4) and IIIA-N2 (22) NSCLC based on SEER data. Further, we found that VPI is associated with poor prognosis in N2 stage NSCLC. The cutoff point of examined lymph nodes are mostly based on our previous studies (20,21). A cutoff point of 3 positive lymph nodes was recommended (18). Therefore, age, sex, number of examined lymph nodes, number of positive lymph nodes, tumor size, extent of surgery, differentiation grade, and VPI were the factors ultimately included in the nomogram.

The calibration plots in the training and external validation cohorts showed ideal agreement between actual OS and the nomogram-predicted OS, indicating that the predictive functionality of the nomograms was excellent. The C-index for our nomograms—0.63 and 0.66 for the PORT and non-PORT cohorts, respectively—were superior to those of TNM staging (0.56 and 0.55, respectively) for OS, with a P value of less than 0.001. Therefore, by combining multiple clinical risk factors, our nomogram have a better discrimination ability than the TNM staging system. Moreover, considering that the data were gathered from the United States' multicenter SEER database and two centers in China—which might reduce the impact of patient history backgrounds and hospital differences—the nomograms can be generally applied.

Although several NSCLC prognostic models had been reported previously (20-24), no nomogram had been developed for completely resected pathologic N2 NSCLC with and without PORT. We had previously developed a survival model to predict OS for patients with stage I–IIIA resected NSCLC, but only 24% of the cases included were N2 and it was not related to PORT (20). A recent study proposed a nomogram to predict the survival of patients with stage IIIA–N2 NSCLC after surgery (22); however, it lacked chemotherapy data and could not guide the choice of PORT. Jiang *et al.* (25) reported a similar survival prediction model for patients with stage II or III gastric cancer. Their nomograms can be applied to calculate individualized predictions of the probable OS advantage from adjuvant chemotherapy for these patients. We also established practical nomograms to predict OS and identified a subset of patients who might benefit from PORT.

There are some limitations to our study. First, the clinical characteristics of patients with and without PORT differed slightly between the training and external validation cohorts (*Table 1*); in particular, only a very low proportion of the Chinese patients had received PORT. Therefore, our results should be further validated using large multicenter data from other countries. Second, our study was limited by its retrospective design, which introduced unavoidable bias. The only way to solve this issue is by carrying out a well-conducted phase III trial. Further, our study lacked data on some relevant molecular factors, the chemotherapy regimen and cycle, tumor recurrence, DFS, radiotherapy details, surgical margin status, and comorbidity. Moreover, the C-indices of the nomogram were only 0.619 and 0.627, which is not inspiring. Future studies using prospective data collection and additional prognostic variables are needed to improve the performance and reliability of the model.

Conclusions

We have established a practical nomogram that can produce an individualized estimate of the net survival difference with or without PORT for patients with completely resected pathologic N2 NSCLC who have received chemotherapy. This model can help to quantify the survival benefit of PORT after surgical resection of N2 NSCLC with chemotherapy and can assist in making individualized therapeutic decisions.

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Footnote

Reporting Checklist: The authors have completed the TRIPOD reporting checklist. Available at https://jtd.amegroups.com/article/view/10.21037/jtd-22-772/rc

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jtd.amegroups.com/article/view/10.21037/jtd-22-772/coif). JH serves as Executive Editor-in-Chief of the *Journal of Thoracic Disease*. WL served as an unpaid editorial board member of

the *Journal of Thoracic Disease*. The other authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The Ethics Committee of the First Affiliated Hospital of Guangzhou Medical University approved this study (approval No. 2020 No. 69; issued date 13/3/2020). Individual consent for this retrospective analysis was waived.

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Supplementary

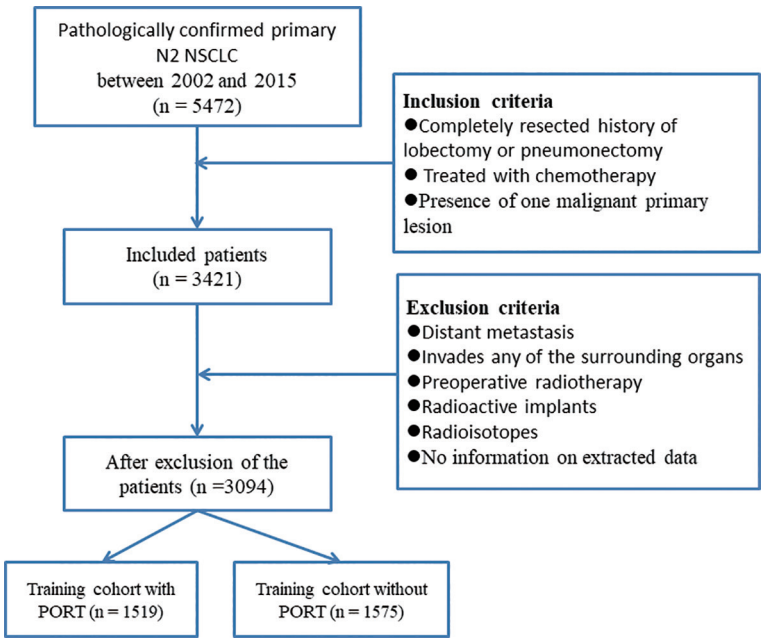

Figure S1 Flowchart of study development. NSCLC, non-small cell lung cancer; PORT, postoperative radiotherapy.

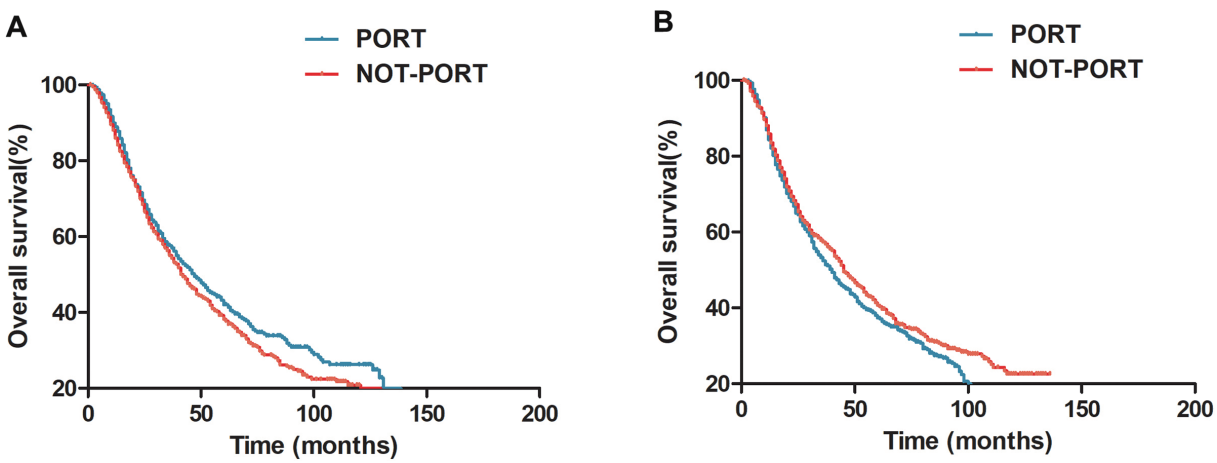

Figure S2 Kaplan-Meier estimates of OS for patients with a positive PORT net survival difference (A) and patients with a negative PORT net survival difference (B). PORT, postoperative radiotherapy; OS, overall survival.

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