

Supplementary

Table S1 Univariate and multivariate Cox regression analysis for 8th edition TNM stage by stratified analysis of histotype, adjusted by race, gender, age, surgery, number of regional lymph nodes removed, radiotherapy and adjuvant chemotherapy

Variables	Univariate analysis		Variables	Multivariate analysis	
	HR (95% CI)	P value		HR (95% CI)	P value
G1					
IA1 as reference			IA1 as reference		
IA2	0.66(0.45, 0.98)	0.04	IA2	0.74(0.50, 1.11)	0.14
IA3	0.44(0.27, 0.72)	<0.01	IA3	0.53(0.32, 0.89)	0.01
IB	0.78(0.50, 1.22)	0.27	IB	1.25(0.78, 2.01)	0.36
IIA	1.01(0.50, 2.04)	0.97	IIA	1.60(0.78, 3.28)	0.20
IIB	0.95(0.56, 1.60)	0.83	IIB	1.51(0.86, 2.64)	0.15
IIIA	1.70(1.00, 2.88)	0.05	IIIA	2.23(1.27, 3.91)	0.01
IIIB	2.71(0.96, 7.61)	0.06	IIIB	2.36(0.72, 7.72)	0.16
G2					
G1 as reference			T1 as reference		
IA2	1.57(0.46, 5.33)	0.47	IA2	0.99(0.26, 3.80)	0.98
IA3	0.75(0.19, 2.92)	0.68	IA3	0.51(0.12, 2.22)	0.37
IB	0.80(0.20, 3.20)	0.75	IB	0.72(0.16, 3.18)	0.67
IIA	0.00(0.00, 1.471E+262)	0.97	IIA	0.00(0.00, 2.042E+278)	0.97
IIB	1.70(0.47, 6.10)	0.42	IIB	2.07(0.55, 7.88)	0.28
IIIA	1.87(0.54, 6.52)	0.33	IIIA	2.16(0.53, 8.74)	0.28
IIIB	3.30(0.55, 19.85)	0.19	IIIB	3.76 (0.49, 28.77)	0.20
G3					
IA1 as reference			T1 as reference		
IA2	0.97(0.56, 1.71)	0.93	IA2	1.08(0.62, 1.91)	0.78
IA3	1.20(0.68, 2.14)	0.53	IA3	1.30(0.72, 2.33)	0.39
IB	1.03(0.57, 1.86)	0.91	IB	1.32(0.72, 2.40)	0.37
IIA	0.78(0.36, 1.69)	0.53	IIA	1.03(0.46, 2.31)	0.94
IIB	1.62(0.92, 2.85)	0.10	IIB	2.65(1.45, 4.85)	<0.01
IIIA	1.52(0.87, 2.66)	0.14	IIIA	2.35(1.28, 4.31)	<0.01
IIIB	2.11(0.86, 5.18)	0.10	IIIB	4.06(1.55, 10.66)	<0.01

G1, low-grade typical pulmonary carcinoids; G2 intermediate-grade atypical pulmonary carcinoids; G3, high-grade large cell neuroendocrine carcinomas.

Table S2 Comparison of univariate Cox regression analysis and survival prediction ability for the already published classification and new stage

Stage	Already published classification		Stage	New-Ed.		New-Ed. vs already published classification	
	HR(95%CI)	C-index (95%CI)		HR (95% CI)	C-index(95%CI)	NRI(95%CI)	IDI(% ,95%CI)
SEER cohort							
IA as reference		0.75 (0.73,0.76)	IA as reference		0.75(0.74, 0.76)	0.03(<-0.01, 0.38)	-0.6(-1.7, 0.7)
IB***	2.09(1.56,2.81)		IB***	1.99(1.62, 2.45)			
IIA***	2.05(1.58,2.67)		II***	6.53(5.74, 7.42)			
IIB***	4.29(3.17,5.79)		III***	12.74(10.72, 15.15)			
IIIA***	7.06(6.18,8.06)						
IIIB***	8.99(6.13,13.17)						
IIIC***	12.04(10.16, 14.28)						
Shanghai cohort							
IA as reference		- ^a	IA as reference		0.80(0.71, 0.88)	-0.1 ^{3b}	-1.7(-14.2, 1.4)
IB	0.00(0.00, -7.98E+307)		IB	10.73(0.67, 171.52)			
IIA	13.20(0.83,211.22)		II	8.36(0.93, 75.03)			
IIB ^c			III***	35.18(4.51, 274.20)			
IIIA	5.76(0.52, 63.64)						
IIIB**	36.97(3.30, 414.47)						
IIIC**	36.15(4.64, 281.86)						

IDI, integrated discrimination improvement; NRI, net reclassification index. *, p< 0.05; **, p<0.01; ***, p< 0.001. ^a, coefficient may be infinite in the cox model due to little outcome events which may cause data bias; ^b, cox model can't be established due to little outcome events for which 95% CI can't be analyzed by bootstrapping; ^c, no patients in the already published classification stage IIB in the Shanghai cohort.

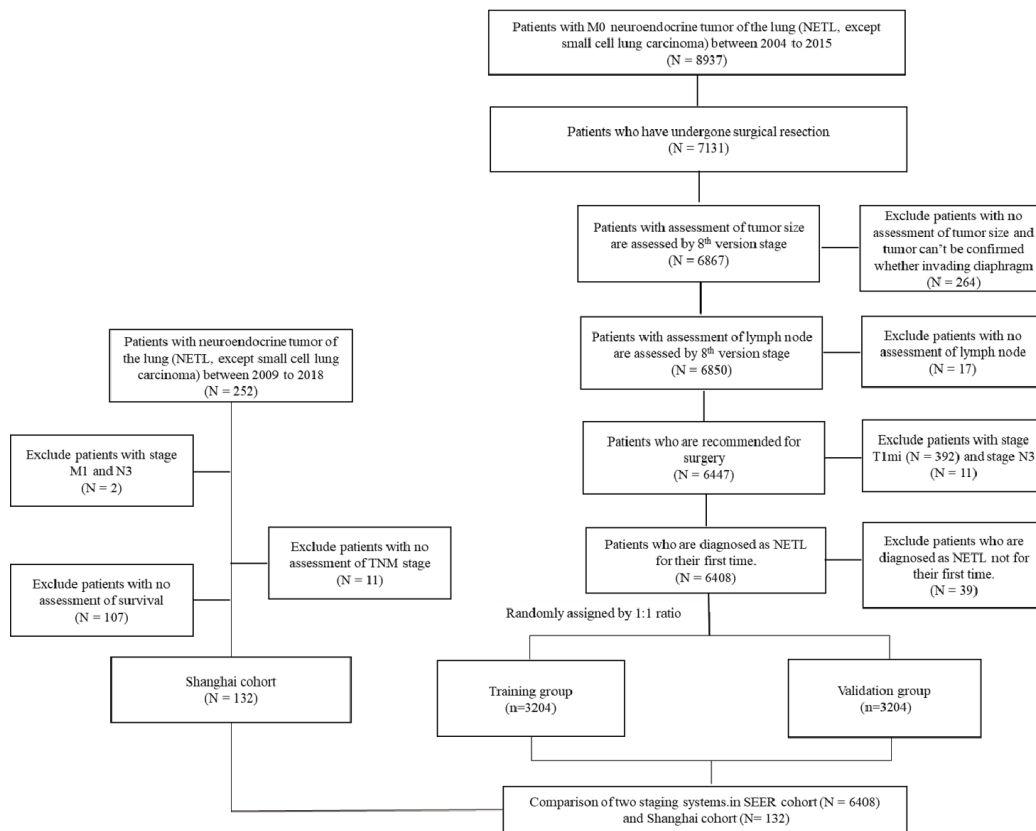


Figure S1 Flow chart depicting selection criteria and grouping steps.

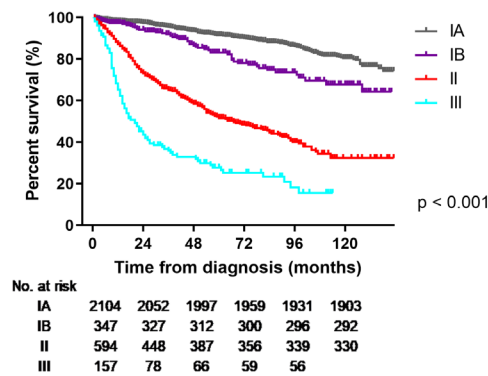


Figure S2 Overall survival by pathologic stage according to the new pathological staging system in the SEER validation group.

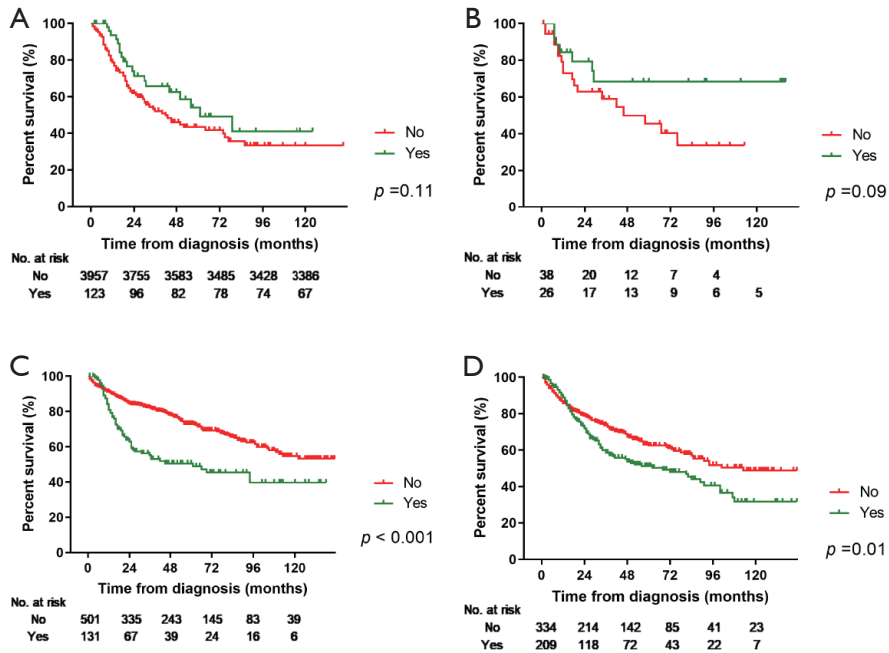


Figure S3 Overall survival by adjuvant chemotherapy according to the TNM staging system. (A) Stage IA, (B) stage IB, (C) stage II, and (D) stage III in the SEER cohort.

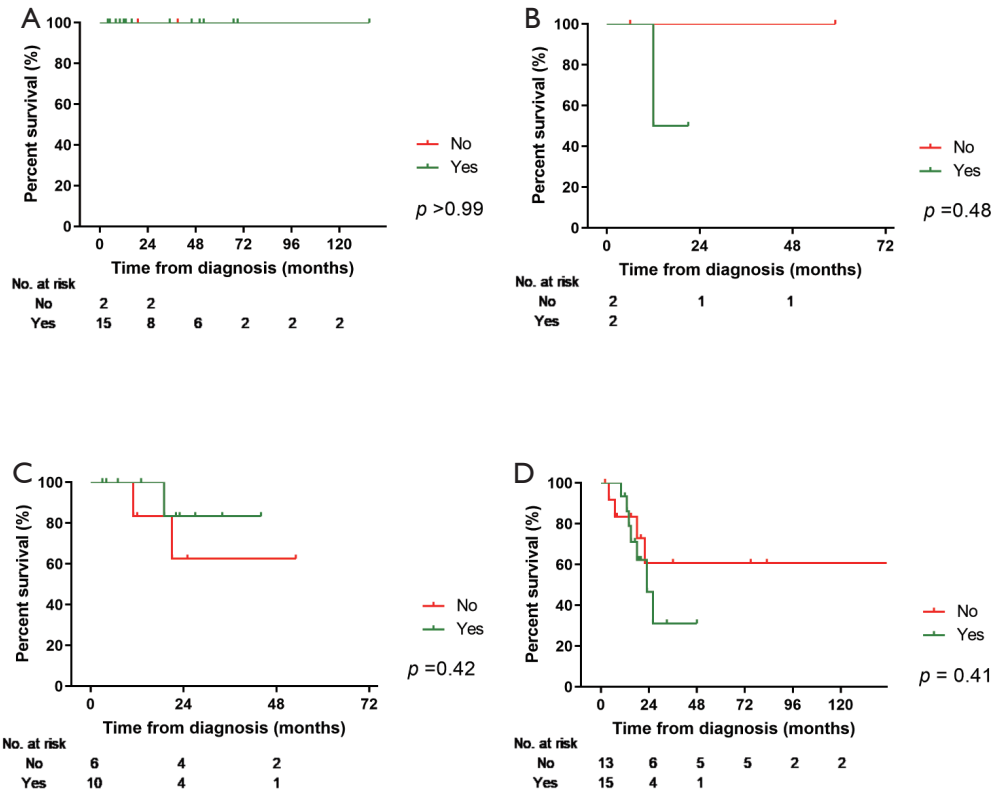


Figure S4 Overall survival by adjuvant chemotherapy according to the TNM staging system. (A) Stage IA, (B) stage IB, (C) stage II, and (D) stage III in the Shanghai cohort.

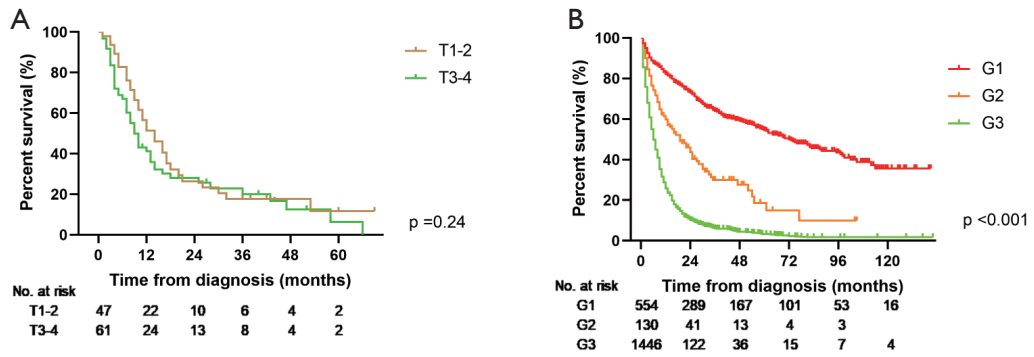


Figure S5 (A) Overall survival by histotype in patients with stage III C or IV tumors; (B) Overall survival by the T stage in patients with stage III C tumors.