

SUPPLEMENTAL DIGITAL CONTENT 1: Supplemental tables

SUPPLEMENTAL TABLE 1. Number of Non-Small Cell Lung Cancer Cases Analyzed by Geographic Region And Type of Staging

Region	Clinically staged M0					Pathologically staged M0*				
	Total	cT1	cT2	cT3	cT4	Total	pT1	pT2	pT3	pT4
North and South America	75	31	36	8	0	2577	1364	994	194	25
Australia	1375	752	429	146	48	1032	454	460	112	6
Europe	1268	383	456	251	178	2571	745	1259	475	92
Asia	10294	5934	3318	900	142	23838	10805	9915	2839	279
Total	13012	7100	4239	1305	368	30018	13368	12628	3620	402

* It includes patients who also have clinically staged tumors

SUPPLEMENTAL TABLE 2. Clinical and Pathologic T Categories by Histological Type

Histological type	Clinically staged M0					Pathologically staged M0				
	Total	cT1	cT2	cT3	cT4	Total	pT1	pT2	pT3	pT4
Adenocarcinoma	8279	5397	2235	521	126	19101	9904	7331	1718	148
Bronchioloalveolar	182	127	40	10	5	372	217	94	52	9
Adeno-squamous	249	109	102	35	3	447	135	234	70	8
Large cell, NOS	419	172	149	77	21	1086	317	518	231	20
Large cell neuroendocrine	48	20	18	9	1	130	86	37	7	0
NSC NOS, Mixed	400	140	167	58	35	463	183	215	56	9
NSC, Other	81	35	22	14	10	50	24	22	2	2
Sarcomatoid	121	29	49	37	6	135	22	72	33	8
Squamous	3233	1071	1457	544	161	8234	2480	4105	1451	198
Total	13012	7100	4239	1305	368	30018	13368	12628	3620	402

NOS: not otherwise specified

SUPPLEMENTAL TABLE 3. Summary of Non-Small Cell Lung Cancer Cases Analyzed by Pathologic T and Completeness of Resection

		Pathologic T				Total
		pT1	pT2	pT3	pT4	
Any pN	Sufficient T Information	13368	12628	3620	402	30018
	R0	12829	11902	3140	279	28150
	R1	206	326	173	35	740
	R2	173	220	218	72	683
	R1/R2	13	32	21	6	72
	No Information	147	148	68	10	373
pN0	Sufficient T Information	11559	8411	2108	179	22257
	R0	11159	8082	1882	126	21249
	R1	144	150	89	13	396
	R2	118	73	95	33	319
	R1/R2	7	13	8	0	28
	No Information	131	93	34	7	265

R0: no residual tumor; R1: microscopic residual tumor; R2: macroscopic residual tumor

SUPPLEMENTAL TABLE 4. Results of Multivariate Analyses of Survival of Pathologically Staged T1-3 N0M0R0 Cases According to Tumor Size

Variable	n/N (%)	Survival from Surgery	
		HR (95% CI)	P-value
Age >= 60 vs. <60	15989/20910 (76%)	2.04 (1.88, 2.22)	<.001
Americas vs. Asia	1867/20910 (9%)	1.85 (1.68, 2.03)	<.001
Europe/Aus vs. Asia	2346/20910 (11%)	2.13 (1.98, 2.29)	<.001
Male vs. Female	12404/20910 (59%)	1.63 (1.53, 1.74)	<.001
Other Histology vs. adenocarcinoma	6984/20910 (33%)	1.35 (1.27, 1.43)	<.001
Size >2 cm vs. <= 2 cm	12856/20910 (61%)	1.30 (1.20, 1.40)	<.001
Size >3 cm vs. >2-3 cm	7097/20910 (34%)	1.28 (1.18, 1.39)	<.001
Size >5 cm vs. >3-5 cm	1914/20910 (9%)	1.15 (1.03, 1.29)	0.016
Size >7 cm vs. >5-7 cm	603/20910 (3%)	1.40 (1.22, 1.61)	<.001
Size >1 cm vs. <=1 cm	19440/20910 (93%)	1.58 (1.33, 1.87)	<.001
Size >4 cm vs. <= 4 cm	3644/20910 (17%)	1.22 (1.11, 1.35)	<.001

HR- Hazard Ratio, 95% CI- 95% Confidence Interval, P-value from Wald Chi-Square Test in Cox Regression
n/N (%): n=number with descriptor, N=number evaluated, %=percent with descriptor.

SUPPLEMENTAL TABLE 5. Results of Univariate Analyses of Survival of Clinically Staged T1-3 N0M0R0 Cases According to Tumor Size and T2 and T3 descriptors

Variable	n/N (%)	Survival from diagnosis	
		HR (95% CI)	P-value
Other histology vs. adenocarcinoma	3039/10078 (30%)	2.09 (1.93,2.26)	<.001
Squamous vs. other	2079/10078 (21%)	1.83 (1.68,2.00)	<.001
Age >= 60 vs. <60	7776/10057 (77%)	1.86 (1.67,2.08)	<.001
Male vs. female	6004/10062 (60%)	2.06 (1.88,2.25)	<.001
Americas vs. Asia	892/10081 (9%)	1.67 (1.47,1.89)	<.001
Europe/Aus vs. Asia	706/10081 (7%)	2.40 (2.06,2.79)	<.001
Size >2 cm vs. </=2 cm	5955/10081 (59%)	1.61 (1.44,1.79)	<.001
Size >3 cm vs. >2-3 cm	3240/10081 (32%)	1.50 (1.35,1.66)	<.001
Size >5 cm vs. >3-5 cm	770/10081 (8%)	1.69 (1.46,1.96)	<.001
Size >7 cm vs. >5-7	253/10081 (3%)	1.63 (1.32,2.00)	<.001
Size >1 cm vs. </= 1cm	9268/10078 (92%)	3.20 (2.54,4.02)	<.001
Size >4 cm vs. </= 4 cm	1468/10078 (15%)	2.67 (2.44,2.92)	<.001
Size >6 cm vs. </= 6 cm	435/10078 (4%)	3.67 (3.21,4.20)	<.001
Multiple cT2 descriptors vs. single cT2 descriptors, cT3	198/3602 (5%)	0.98 (0.77,1.25)	0.902
cT3 vs. cT1-2	718/10078 (7%)	3.05 (2.72,3.42)	<.001
cT2 Main bronchus > 2 cm vs. all others	44/9616 (0%)	1.81 (1.11,2.96)	0.018
cT3 Main bronchus < 2cm vs. all others	23/9616 (0%)	2.05 (1.02,4.10)	0.043
cT2 Atelectasis vs. all others	143/9629 (1%)	2.31 (1.76,3.02)	<.001
cT3 Atelectasis vs. all others	6/9629 (0%)	1.30 (0.18,9.23)	0.793
cT2 >3-5 cm size only vs.cT1, cT2 <=3 cm	2079/10081 (21%)	1.87 (1.70,2.05)	<.001
cT2 >3-5 cm plus other descriptor vs.cT1, cT2 <=3 cm	178/10081 (2%)	2.15 (1.66,2.78)	<.001
cT2>5-7 cm size only vs.cT1, cT2 <=3 cm	336/10081 (3%)	3.11 (2.61,3.70)	<.001
cT2>5-7 cm plus other descriptor vs.cT1, cT2 <=3 cm	57/10081 (1%)	3.22 (2.15,4.82)	<.001
cT3 Single descriptor vs.cT1, cT2 <=3 cm	486/10081 (5%)	3.63 (3.14,4.20)	<.001
cT3 Multiple descriptors vs.cT1, cT2 <=3 cm	233/10081 (2%)	4.33 (3.61,5.20)	<.001

HR- Hazard Ratio, 95% CI- 95% Confidence Interval, P-value from Wald Chi-Square Test in Cox Regression
n/N (%): n=number with descriptor, N=number evaluated, %=percent with descriptor.

SUPPLEMENTAL TABLE 6. Multivariate Survival Analyses of Clinically Staged Tumors According to 7th Edition Tumor Sizes and Proposed New Cutpoints

Variable	n/N (%)	Survival from diagnosis	
		HR (95% CI)	P-value
Age >= 60 vs. < 60	7776/10057 (77%)	1.67 (1.49,1.87)	<.001
Americas vs. Asia	890/10057 (9%)	1.67 (1.46,1.90)	<.001
Europe/Aus vs. Asia	690/10057 (7%)	1.73 (1.48,2.02)	<.001
Male vs. female	6001/10057 (60%)	1.68 (1.53,1.84)	<.001
Other histology vs. adeno	3023/10057 (30%)	1.30 (1.20,1.42)	<.001
Size >2 cm vs. </= 2 cm	5936/10057 (59%)	1.40 (1.25,1.57)	<.001
Size >3 cm vs.>2-3 cm	3228/10057 (32%)	1.27 (1.13,1.43)	<.001
Size >5 cm vs. >3-5 cm	766/10057 (8%)	1.32 (1.11,1.58)	0.002
Size >7 cm vs. >5-7 cm	252/10057 (3%)	1.59 (1.29,1.96)	<.001
Size >1 cm vs. <= 1 cm	9248/10057 (92%)	1.79 (1.41,2.28)	<.001
Size >4 cm vs. <=4 cm	1461/10057 (15%)	1.22 (1.05,1.41)	0.008

HR- Hazard Ratio, 95% CI- 95% Confidence Interval, P-value from Wald Chi-Square Test in Cox Regression

n/N (%): n=number with descriptor, N=number evaluated, %=percent with descriptor.

Note: similar to the analyses of pathologically staged tumors, the 6 cm cutpoint was not significant after adjusting for the other size cutpoints.

SUPPLEMENTAL TABLE 7. Multivariate Survival Analyses of Proposed 1-cm Cutpoints in Clinically Staged T1 Tumors

Survival from diagnosis			
Variable	n/N (%)	HR (95% CI)	P-value
Age >= 60 vs. <60	6766/8763 (77%)	1.70 (1.49,1.93)	<.001
Americas vs. Asia	773/8763 (9%)	1.82 (1.57,2.11)	<.001
Europe/Aus vs. Asia	486/8763 (6%)	1.74 (1.41,2.14)	<.001
Male vs. female	4976/8763 (57%)	1.71 (1.54,1.89)	<.001
Other histology vs. adenocarcinoma	2313/8763 (26%)	1.51 (1.30,1.74)	<.001
Squamous vs. other	1560/8763 (18%)	0.84 (0.71,0.98)	0.030
T1a >1-2 cm vs. <= 1cm	3167/8763 (36%)	1.79 (1.39,2.29)	<.001
T1b >2-3 cm vs. < 1 cm	2468/8763 (28%)	2.56 (2.00,3.28)	<.001
T2a <3 cm vs. < 1 cm	2338/8763 (27%)	3.38 (2.64,4.32)	<.001

HR- Hazard Ratio, 95% CI- 95% Confidence Interval, P-value from Wald Chi-Square Test in Cox Regression
n/N (%): n=number with descriptor, N=number evaluated, %=percent with descriptor.

Note: similar to the survival analyses of pathologically staged tumors, the current and proposed risk groups distinguish between risk groups. A comparison of T2a <3 cm (T2a by other descriptors other than size) vs. larger T1 cases (T1b >2-3 cm, not shown in table,) indicates that T2a cases are appropriately in a higher risk category.

SUPPLEMENTAL TABLE 8. Survival Comparisons of Clinically Staged T2-4 Tumors >4-5 cm, >5-7 cm and > 7 cm in Greatest Dimension

		Survival from diagnosis		
	Variable	n/N (%)	HR (95% CI)	P-value
Univariate	Other histology vs. adeno	1697/3777 (45%)	1.50 (1.35,1.67)	<.001
	Squamous vs. other	1219/3777 (32%)	1.30 (1.16,1.45)	<.001
	Age >= 60 vs.<60	3001/3764 (80%)	1.47 (1.27,1.71)	<.001
	Male vs. female	2643/3766 (70%)	1.78 (1.56,2.02)	<.001
	Americas vs. Asia	308/3777 (8%)	1.12 (0.92,1.37)	0.260
	Europe/Aus vs. Asia	460/3777 (12%)	1.89 (1.60,2.23)	<.001
	Proposed T2b (4-5 cm) vs.all others	606/3777 (16%)	0.99 (0.86,1.14)	0.901
	Proposed T3 (5-7 cm) vs.all others	552/3777 (15%)	1.47 (1.28,1.69)	<.001
	T3 (Excluding >7 cm) vs.all others	271/3777 (7%)	1.20 (0.98,1.47)	0.070
	Proposed T4 (including >7 cm) vs.all others	414/3777 (11%)	2.23 (1.93,2.58)	<.001
Multivariate	Other histology vs. adeno	1687/3764 (45%)	1.34 (1.14,1.58)	<.001
	Squamous vs. other	1212/3764 (32%)	0.80 (0.67,0.95)	0.010
	Age >= 60 vs. <60	3001/3764 (80%)	1.59 (1.37,1.85)	<.001
	Male vs. female	2643/3764 (70%)	1.57 (1.37,1.80)	<.001
	Americas vs.Asia	308/3764 (8%)	1.10 (0.89,1.37)	0.356
	Europe/Aus vs.Asia	449/3764 (12%)	1.49 (1.25,1.78)	<.001
	Proposed T2B (4-5 cm) vs. T2 3-4 cm	602/3764 (16%)	1.26 (1.08,1.47)	0.004
	Proposed T3 (5-7 cm) vs. T2 3-4 cm	549/3764 (15%)	1.70 (1.46,1.98)	<.001
	T3 (Excluding >7 cm) vs.T2 3-4 cm	271/3764 (7%)	1.47 (1.19,1.81)	<.001
Proposed T4 (including >7 cm) vs.T2 3-4 cm	413/3764 (11%)	2.41 (2.05,2.83)	<.001	

HR- Hazard Ratio, 95% CI- 95% Confidence Interval, P-value from Wald Chi-Square Test in Cox Regression
n/N (%): n=number with descriptor, N=number evaluated, %=percent with descriptor.

Note: specific comparisons not shown in table: when the survival of tumors >5-7 cm is compared with that of tumors >4-5 cm, the p value is 0.0015, indicating that survival is different between the two groups. When the survival of T3 tumors (excluding those > 7 cm) is compared with that of >5-7 cm tumors, the p value is 0.219, indicating that survival is similar for those groups. (Data not shown on the table)

SUPPLEMENTAL TABLE 9. Univariate Analyses of Survival for Pathologically Staged T3 and T4 Tumors

Variable	n/N (%)	Survival from surgery	
		HR (95% CI)	P-value
Other histology vs. adenocarcinoma	1078/2008 (54%)	1.28 (1.12, 1.46)	<.001
Squamous vs. other	791/2008 (39%)	1.30 (1.14, 1.48)	<.001
Age >= 60 vs. <60	1568/2005 (78%)	1.83 (1.53, 2.20)	<.001
Male vs. female	1469/1996 (74%)	1.24 (1.06, 1.45)	0.006
Americas vs. Asia	140/2008 (7%)	0.94 (0.69, 1.27)	0.6823
Europe/Aus vs. Asia	332/2008 (17%)	1.75 (1.48, 2.06)	<.0001
Any pT4 vs.pT3	126/2008 (6%)	1.07 (0.81, 1.40)	0.645
pT3 > 7 cm vs.other pT3, pT4	535/2008 (27%)	1.33 (1.15, 1.53)	<.001
pT3 Parietal Pericardium vs.other pT3, pT4	25/2008 (1%)	1.39 (0.80, 2.40)	0.238
pT3 Diaphragm vs.other pT3, pT4	40/2008 (2%)	1.84 (1.25, 2.72)	0.002
pT3 Mediastinal pleura vs.other pT3, pT4	59/2008 (3%)	1.41 (0.99, 2.01)	0.056
Multiple vs. single descriptor pT3, pT4	326/2008 (16%)	1.34 (1.13, 1.58)	<.001

HR- Hazard Ratio, 95% CI- 95% Confidence Interval, P-value from Wald Chi-Square Test in Cox Regression
n/N (%): n=number with descriptor, N=number evaluated, %=percent with descriptor.

SUPPLEMENTAL TABLE 10. Multivariate Analyses of Survival for Pathologically Staged T3 and T4 Tumors

Variable	n/N (%)	Survival from Surgery	
		HR (95% CI)	P-value
Other histology vs. adenocarcinoma	1069/1994 (54%)	1.05 (0.85, 1.30)	0.630
Squamous vs. other	785/1994 (39%)	1.14 (0.92, 1.40)	0.229
Age >= 60 vs. <60	1558/1994 (78%)	1.84 (1.53, 2.21)	<.001
Male vs. female	1467/1994 (74%)	1.34 (1.14, 1.58)	<.001
Americas vs. Asia	140/1994 (7%)	0.96 (0.70, 1.31)	0.806
Europe/Aus vs. Asia	331/1994 (17%)	1.78 (1.48, 2.12)	<.001
pT3 > 7 cm vs. pT3 other than 7 cm	532/1994 (27%)	1.19 (1.02, 1.39)	0.026
Any pT4 vs. pT3 other than 7 cm	125/1994 (6%)	1.08 (0.81, 1.43)	0.604

HR- Hazard Ratio, 95% CI- 95% Confidence Interval, P-value from Wald Chi-Square Test in Cox Regression
n/N (%): n=number with descriptor, N=number evaluated, %=percent with descriptor.

Note: In the pathologically staged population, pT3 other than 7 cm and pT4 tumors are not significantly different ($p = 0.604$). pT3 > 7 cm is significantly different from other pT3 tumors with other descriptors ($p = 0.026$), but it is not significantly different from pT4 tumors ($p = 0.51$, not shown in table).

SUPPLEMENTAL TABLE 11. Univariate Analyses of Survival for Clinically Staged T3 and T4 Tumors*

		Survival from diagnosis		
Variable	n/N (%)	HR (95% CI)	P-value	
	Other histology vs. adenocarcinoma	485/867 (56%)	1.30 (1.06, 1.58)	0.010
	Squamous vs. other	329/867 (38%)	1.21 (0.99, 1.48)	0.058
	Age >= 60 vs. <60	637/864 (74%)	1.51 (1.19, 1.91)	<.001
	Male vs. female	701/864 (81%)	1.50 (1.14, 1.96)	0.003
	Americas vs. Asia	97/868 (11%)	1.02 (0.72,1.45)	0.9216
	Europe/Aus vs. Asia	188/868 (22%)	1.37 (1.07,1.77)	0.0140
	Any cT4 vs. cT3	149/867 (17%)	0.97 (0.74, 1.27)	0.815
Not provide	cT3 > 7 cm vs.other cT3, cT4	251/867 (29%)	1.60 (1.31, 1.97)	<.001
	cT3 other than Size vs.other cT3, cT4	467/867 (54%)	0.68 (0.56, 0.83)	<.001
	cT3 parietal pericardium vs.other cT3, cT4	10/867 (1%)	1.10 (0.46, 2.66)	0.832
	cT3 Diaphragm vs.other cT3, cT4	18/867 (2%)	1.54 (0.86, 2.73)	0.144
	cT3 Mediastinal Pleura vs.other cT3, cT4	62/867 (7%)	0.83 (0.56, 1.23)	0.361

HR- Hazard Ratio, 95% CI- 95% Confidence Interval, P-value from Wald Chi-Square Test in Cox Regression
n/N (%): n=number with descriptor, N=number evaluated, %=percent with descriptor.

* The discrepancy between the submitted and the analyzed tumors derives from the fact that cases were excluded from the analyzed group if they did not provide T descriptor information supporting the reported T category.

SUPPLEMENTAL TABLE 12. Multivariate Analyses of Survival for Clinically Staged T3 and T4 Tumors

Variable	n/N (%)	Survival from diagnosis	
		HR (95% CI)	P-value
Other histology vs. adenocarcinoma	482/864 (56%)	1.27 (0.95, 1.69)	0.104
Squamous vs. other	328/864 (38%)	0.88 (0.65, 1.18)	0.393
Age >= 60 vs. <60	637/864 (74%)	1.49 (1.17, 1.90)	0.001
Male vs. female	701/864 (81%)	1.48 (1.12, 1.96)	0.007
Americas vs. Asia	96/864 (11%)	1.07 (0.75, 1.55)	0.701
Europe/Aus vs. Asia	185/864 (21%)	1.35 (1.03, 1.76)	0.029
cT3 > 7cm vs. cT3 other than 7 cm	251/864 (29%)	1.61 (1.29, 2.00)	<.001
Any cT4 vs. cT3 other than 7 cm	148/864 (17%)	1.09 (0.81, 1.47)	0.560

HR- Hazard Ratio, 95% CI- 95% Confidence Interval, P-value from Wald Chi-Square Test in Cox Regression

n/N (%): n=number with descriptor, N=number evaluated, %=percent with descriptor.

Note: In the clinically staged population, cT3 other than 7 cm and cT4 tumors are not significantly different ($p = 0.56$). cT3 > 7cm is significantly different from other cT3 tumors with other descriptors ($p < 0.001$), and it is also significantly different from cT4tumors ($p = 0.014$, data not shown in table). This last result differs from the path analysis.

SUPPLEMENTAL TABLE 13. Multivariate Survival Analyses of Clinically Staged Tumors Based on Their Endobronchial Location

Variable	n/N (%)	Survival from diagnosis	
		HR (95% CI)	P-value
Other histology vs. adenocarcinoma	1559/3544 (44%)	1.39 (1.17,1.65)	<.001
Squamous vs. other	1142/3544 (32%)	0.78 (0.65,0.93)	0.006
Age >= 60 vs. <60	2846/3544 (80%)	1.66 (1.42,1.95)	<.001
Male vs. female	2476/3544 (70%)	1.51 (1.31,1.73)	<.001
Americas vs. Asia	253/3544 (7%)	1.09 (0.86,1.39)	0.459
Europe/Aus vs. Asia	351/3544 (10%)	1.57 (1.29,1.92)	<.001
Size >2 cm vs. <= 2 cm	3381/3544 (95%)	0.88 (0.61,1.27)	0.492
Size >3 cm vs. 2-<=3 cm	3148/3544 (89%)	1.25 (0.96,1.61)	0.093
Size >5 cm vs. 3-<=5 cm	721/3544 (20%)	1.51 (1.29,1.75)	<.001
Size >7 cm vs.5-<=7 cm	226/3544 (6%)	1.10 (0.85,1.42)	0.459
cT2 main bronchus > 2cm from carina vs. cT2 without invasion	44/3544 (1%)	1.23 (0.74,2.04)	0.427
cT3 main bronchus <2cm from carina vs.cT2 without invasion	23/3544 (1%)	0.96 (0.48,1.93)	0.902
cT3 other than main bronchus vs.cT2, without invasion of main bronchus	645/3544 (18%)	1.51 (1.27,1.79)	<.001

HR- Hazard Ratio, 95% CI- 95% Confidence Interval, P-value from Wald Chi-Square Test in Cox Regression
n/N (%): n=number with descriptor, N=number evaluated, %=percent with descriptor.

SUPPLEMENTAL TABLE 14. Multivariate survival Analyses of Pathologically Staged T2 and T3 Tumors Based on Partial or Total Lung Atelectasis/Pneumonitis

Variable	n/N (%)	Survival from surgery	
		HR (95% CI)	P-value
Other histology vs. adeno	2381/5561 (43%)	1.26 (1.08,1.47)	0.004
Squamous vs. other	1797/5561 (32%)	0.93 (0.80,1.09)	0.373
Age >= 60 vs. <60	4382/5561 (79%)	1.93 (1.68,2.22)	<.001
Male vs. female	3567/5561 (64%)	1.35 (1.21,1.50)	<.001
Americas vs.Asia	232/5561 (4%)	1.98 (1.56,2.50)	<.001
Europe/Aus vs. Asia	1033/5561 (19%)	2.19 (1.95,2.46)	<.001
Size >2 cm vs.<= 2 cm	4805/5561 (86%)	1.35 (1.11,1.65)	0.003
Size >3 cm vs. 2-<=3 cm	3880/5561 (70%)	1.04 (0.91,1.20)	0.546
Size >5 cm vs. 3-<=5 cm	1018/5561 (18%)	1.38 (1.21,1.58)	<.001
Size >7 cm vs. 5-<=7 cm	296/5561 (5%)	1.03 (0.82,1.28)	0.816
pT2 partial atelectasis vs.other pT2	145/5561 (3%)	1.10 (0.82,1.47)	0.511
pT3 total atelectasis vs.pT2	7/5561 (0%)	1.76 (0.44,7.09)	0.428
pT3 other than atelectasis vs.pT2	983/5561 (18%)	1.65 (1.44,1.88)	<.001

HR- Hazard Ratio, 95% CI- 95% Confidence Interval, P-value from Wald Chi-Square Test in Cox Regression
n/N (%): n=number with descriptor, N=number evaluated, %=percent with descriptor.

SUPPLEMENTAL TABLE 15. Multivariate Survival Analyses of Pathologically Staged T1 and T2 Tumors Based on the Status of the Visceral Pleura *

Variable	n/N (%)	Survival from surgery	
		HR (95% CI)	P-value
Americas vs. Asia	417/15513 (3%)	1.89 (1.53,2.33)	<.001
Europe/Aus vs. Asia	411/15513 (3%)	1.56 (1.21,2.01)	<.001
Male vs. female	9241/15513 (60%)	2.01 (1.84,2.21)	<.001
Age >= 60 vs. <60	11857/15513 (76%)	2.19 (1.95,2.45)	<.001
Other histology vs. adeno	4329/15513 (28%)	1.82 (1.59,2.07)	<.001
Squamous vs. other	3385/15513 (22%)	0.79 (0.69,0.91)	<.001
Size >2 cm vs. <= 2 cm	8972/15513 (58%)	1.40 (1.27,1.54)	<.001
Size >3 cm vs. 2-<=3 cm	4526/15513 (29%)	1.33 (1.21,1.46)	<.001
Size >5 cm vs. 3-<=5 cm	762/15513 (5%)	1.20 (1.05,1.38)	0.008
Visceral pleura invasion vs. no visceral pleura invasion	3344/15513 (22%)	1.51 (1.39,1.63)	<.001

HR- Hazard Ratio, 95% CI- 95% Confidence Interval, P-value from Wald Chi-Square Test in Cox Regression

n/N (%): n=number with descriptor, N=number evaluated, %=percent with descriptor.

* Cases from Electronic Data Collection, Memorial Sloan Kettering Cancer Center and Japan, only.

SUPPLEMENTAL TABLE 16. Multivariate Survival Analyses of Pathologically Staged T1 and T2 Tumors Based on the Extent of the Visceral Pleura Invasion *

Variable	n/N (%)	Survival from surgery	
		HR (95% CI)	P-value
Americas vs. Asia	187/14861 (1%)	2.51 (2.03,3.11)	<.001
Europe/Aus vs. Asia	66/14861 (0%)	0.59 (0.24,1.41)	0.234
Male vs. female	8805/14861 (59%)	1.97 (1.79,2.16)	<.001
Age >= 60 vs. < 60	11369/14861 (77%)	2.24 (1.99,2.53)	<.001
Other histology vs. adeno	3986/14861 (27%)	1.89 (1.65,2.16)	<.001
Squamous vs. other	3191/14861 (21%)	0.77 (0.67,0.88)	<.001
Size >2 cm vs. <=2 cm	8599/14861 (58%)	1.37 (1.24,1.51)	<.001
Size >3 cm vs. 2-<=3 cm	4282/14861 (29%)	1.33 (1.21,1.46)	<.001
Size >5 cm vs. 3-<=5 cm	701/14861 (5%)	1.22 (1.06,1.40)	0.005
Visceral pleura PL1 vs. no invasion	2527/14861 (17%)	1.44 (1.32,1.58)	<.001
Visceral pleura PL2 vs. no invasion	748/14861 (5%)	1.74 (1.51,1.99)	<.001

HR- Hazard Ratio, 95% CI- 95% Confidence Interval, P-value from Wald Chi-Square Test in Cox Regression
n/N (%): n=number with descriptor, N=number evaluated, %=percent with descriptor.

* Cases from Electronic Data Collection, Memorial Sloan Kettering Cancer Center and Japan, only.

Note: test for a difference between PL1 and PL0 is <0.001, indicating that PL1 is different from PL0. Test for a difference between PL1 and PL2 is 0.012, indicating the two levels are important to distinguish. (Data not shown on table)

SUPPLEMENTAL TABLE 17. Multivariate Survival Analyses of Clinically Staged T1 and T2 Tumors Based on the Status of the Visceral Pleura

Variable	n/N (%)	Survival from diagnosis	
		HR (95% CI)	P-value
Americas vs. Asia	480/8916 (5%)	1.25 (1.02,1.55)	0.036
Europe/Aus vs. Asia	520/8916 (6%)	1.92 (1.59,2.31)	<.001
Male vs. female	5237/8916 (59%)	1.76 (1.59,1.96)	<.001
Age >= 60 vs. <60	6882/8916 (77%)	1.69 (1.49,1.92)	<.001
Other histology vs. adeno	2449/8916 (27%)	1.51 (1.30,1.75)	<.001
Squamous vs. other	1736/8916 (19%)	0.84 (0.71,0.98)	0.028
Size >2 cm vs. <=2 cm	5061/8916 (57%)	1.54 (1.37,1.74)	<.001
Size >3 cm vs. 2-<=3 cm	2597/8916 (29%)	1.36 (1.22,1.52)	<.001
Size >5 cm vs. 3-<=5 cm	383/8916 (4%)	1.43 (1.21,1.70)	<.001
Visceral pleura invasion vs. no invasion	388/8916 (4%)	1.26 (1.05,1.52)	0.013

HR- Hazard Ratio, 95% CI- 95% Confidence Interval, P-value from Wald Chi-Square Test in Cox Regression
n/N (%): n=number with descriptor, N=number evaluated, %=percent with descriptor.

SUPPLEMENTAL TABLE 18. Univariate and Multivariate Survival Analyses for Clinically Staged T1, T2, and T3 Tumors Based on the Status of the Visceral Pleura for the Purpose of Assessing Upstaging Based on Visceral Pleura Invasion. (Proposed Size Cutpoints for the 8th Edition)

	Variable	n/N (%)	Time from Diagnosis	
			HR (95% CI)	P-value
Univariate	Other histology vs. adeno	3115/10185 (31%)	2.12 (1.96,2.29)	<.001
	Age >= 60 vs. <60	7845/10163 (77%)	1.79 (1.60,1.99)	<.001
	Male vs. female	6096/10168 (60%)	2.08 (1.91,2.27)	<.001
	Americas vs. Asia	907/10185 (9%)	1.59 (1.40,1.81)	<.001
	Europe/Aus vs. Asia	774/10185 (8%)	2.44 (2.12,2.81)	<.001
	T1b vs. T1a	3157/9771 (32%)	0.56 (0.51,0.62)	<.001
	T1c vs. T1a	2471/9771 (25%)	0.95 (0.86,1.04)	0.283
	T2a VPI, 0.1-1 cm vs. T1a	1/9771 (0%)	0.00 (0.00,946E65)	0.933
	T2a VPI, >1-2 cm vs. T1a	52/9771 (1%)	1.59 (1.00,2.53)	0.049
	T2a VPI, >2-3 cm vs. T1a	123/9771 (1%)	1.19 (0.84,1.68)	0.325
	T2a size only vs. T1a	1627/9771 (17%)	1.42 (1.28,1.57)	<.001
	T2a VPI, >3-4 cm vs. T1a	126/9771 (1%)	1.33 (0.97,1.84)	0.077
	T2b size only vs. T1a	555/9771 (6%)	1.80 (1.56,2.08)	<.001
	T2b VPI, >4-5 cm vs. T1a	51/9771 (1%)	2.09 (1.36,3.21)	<.001
	T3 vs. T1a	823/9771 (8%)	2.62 (2.34,2.94)	<.001
	Multivariate	Other histology vs. adeno	2860/9750 (29%)	1.31 (1.19,1.43)
Age >= 60 vs. <60		7540/9750 (77%)	1.67 (1.49,1.88)	<.001
Male vs. female		5758/9750 (59%)	1.67 (1.52,1.84)	<.001
Americas vs. Asia		852/9750 (9%)	1.72 (1.50,1.97)	<.001
Europe/Aus vs. Asia		638/9750 (7%)	1.71 (1.44,2.03)	<.001
T1b vs. T1a		3154/9750 (32%)	1.84 (1.43,2.37)	<.001
T1c vs. T1a		2466/9750 (25%)	2.60 (2.02,3.35)	<.001
T2a VPI, 0.1-1 cm vs. T1a		1/9750 (0%)	0.00 (0.00,108E77)	0.947
T2a VPI, >1-2 cm vs. T1a		52/9750 (1%)	4.81 (2.86,8.09)	<.001
T2a VPI, >2-3 cm vs. T1a		123/9750 (1%)	3.30 (2.18,5.01)	<.001
T2a size only vs. T1a		1622/9750 (17%)	3.29 (2.55,4.24)	<.001
T2a VPI, >3-4 cm vs. T1a		126/9750 (1%)	3.49 (2.35,5.20)	<.001
T2b size only vs. T1a		551/9750 (6%)	3.96 (3.00,5.22)	<.001
T2b VPI, >4-5 cm vs. T1a		51/9750 (1%)	4.75 (2.90,7.76)	<.001
T3 vs. T1a		820/9750 (8%)	5.25 (4.04,6.84)	<.001

HR- Hazard Ratio, 95% CI- 95% Confidence Interval, P-value from Wald Chi-Square Test in Cox Regression

n/N (%): n=number with descriptor, N=number evaluated, %=percent with descriptor.

Note: specific comparisons not shown in table: T2a 1-2 cm VPI vs. T2a size only, p = 0.1123; T2a appropriate as proposed. T2a >2-3 cm VPI vs. T2a size only, p = 0.9764; T2a appropriate as proposed. T2a >3-4 cm VPI vs. T2a size only, p = 0.7150; does not supports upstaging to T2b. T2a >3-4 cm VPI vs. T2b size only, p = 0.0945; marginal support for upstaging to T2b. T2b >4-5 cm VPI vs. T2b size only, p = 0.0036; supports upstaging to T3. T2b >4-5 cm VPI vs. T3, p = 0.5761; marginal support for upstaging to T3.

SUPPLEMENTAL TABLE 19. Multivariate Survival Analyses of Pathologically Staged T3-4 Tumors based on Invasion of the Diaphragm.

Variable	n/N (%)	Survival from surgery	
		HR (95% CI)	P-value
Other histology vs. adenocarcinoma	1069/1994 (54%)	1.06 (0.86, 1.31)	0.566
Squamous vs. other	785/1994 (39%)	1.12 (0.91, 1.39)	0.271
Age >= 60 vs. <60	1558/1994 (78%)	1.82 (1.51, 2.18)	<.001
Male vs. female	1467/1994 (74%)	1.34 (1.14, 1.57)	<.001
Americas vs. Asia	140/1994 (7%)	1.02 (0.74, 1.39)	0.920
Europe/Aus vs. Asia	331/1994 (17%)	1.91 (1.61, 2.27)	<.001
pT3 Diaphragm vs. Other pT3	40/1994 (2%)	1.79 (1.20, 2.65)	0.004
Any pT4 vs. pT3 other than diaphragm	125/1994 (6%)	1.02 (0.78, 1.35)	0.864

HR- Hazard Ratio, 95% CI- 95% Confidence Interval, P-value from Wald Chi-Square Test in Cox Regression

n/N (%): n=number with descriptor, N=number evaluated, %=percent with descriptor.

Note: p-value for test of pT3 diaphragm vs. pT4 is 0.02, indicating that pT3 diaphragm is higher risk than other pT4 tumors, and it is also higher risk than other pT3 tumors with other descriptors (p=0.004). (Data not shown in table)

SUPPLEMENTAL TABLE 20. Multivariate Survival Analyses of Clinically Staged T4 Tumors Based on Invasion of the Diaphragm.

Variable	n/N (%)	Survival from diagnosis	
		HR (95% CI)	P-value
Other histology vs. adenocarcinoma	482/864 (56%)	1.24 (0.93, 1.65)	0.147
Squamous vs. other	328/864 (38%)	0.87 (0.65, 1.17)	0.364
Age >= 60 vs. <60	637/864 (74%)	1.52 (1.19, 1.94)	<.001
Male vs. female	701/864 (81%)	1.51 (1.14, 2.00)	0.004
Americas vs. Asia	96/864 (11%)	1.11 (0.77, 1.61)	0.563
Europe/Aus s. Asia	185/864 (21%)	1.44 (1.10, 1.88)	0.008
cT3 diaphragm vs. other T3	18/864 (2%)	1.59 (0.88, 2.86)	0.121
Any cT4 vs. cT3 diaphragm	148/864 (17%)	0.91 (0.69, 1.21)	0.532

HR- Hazard Ratio, 95% CI- 95% Confidence Interval, P-value from Wald Chi-Square Test in Cox Regression

n/N (%): n=number with descriptor, N=number evaluated, %=percent with descriptor.

Note: p-value for test of cT3 diaphragm vs. cT4 is 0.09 (data not shown in table), indicating that pT3 diaphragm is similar risk to cT4 tumors.

SUPPLEMENTAL TABLE 21. Multivariate Survival Analyses of Pathologically Staged T2 and T3 Tumors Classified by Single or Multiple T2 and T3 Descriptors.

Variable	n/N (%)	Survival from surgery	
		HR (95% CI)	P-value
Other histology vs. adeno	4274/9877 (43%)	1.36 (1.22,1.52)	<.001
Squamous vs. other	3263/9877 (33%)	0.89 (0.80,1.00)	0.054
Age >= 60 vs. <60	7857/9877 (80%)	2.01 (1.81,2.23)	<.001
Male vs. female	6543/9877 (66%)	1.47 (1.36,1.60)	<.001
Americas vs. Asia	746/9877 (8%)	1.48 (1.29,1.69)	<.001
Europe/Aus vs. Asia	1389/9877 (14%)	1.86 (1.69,2.04)	<.001
Multiple pT2 <3 cm vs. pT2a <=3cm	5/9877 (0%)	1.48 (0.37,5.93)	0.581
>3-5 cm size only vs. pT2a <=3cm	3282/9877 (33%)	1.06 (0.95,1.18)	0.273
>3-5 cm Multiple descriptors vs. pT2a <=3cm	1349/9877 (14%)	1.34 (1.18,1.52)	<.001
>5-7 cm size only vs. pT2a <=3cm	583/9877 (6%)	1.46 (1.24,1.72)	<.001
>5-7 cm Multiple descriptors vs. pT2a <=3cm	448/9877 (5%)	1.44 (1.22,1.71)	<.001
pT3 Single descriptor vs. pT2a <=3cm	1543/9877 (16%)	1.93 (1.72,2.17)	<.001
pT3 Multiple descriptor vs. pT2a <=3cm	326/9877 (3%)	2.27 (1.91,2.71)	<.001

HR- Hazard Ratio, 95% CI- 95% Confidence Interval, P-value from Wald Chi-Square Test in Cox Regression
n/N (%): n=number with descriptor, N=number evaluated, %=percent with descriptor.

Notes: the comparison between pT2a (>3-5 cm) by size only and pT2a by multiple descriptors ($p < 0.001$) indicates that these groups have different risks. This finding may justify upstaging pT2a by multiple descriptors. Additionally, the comparison between pT2a (>3-5 cm) with multiple descriptors and pT2b (>5-7 cm) by size only ($p = 0.29$) indicates that these two groups have similar risks, supporting the upstaging of pT2a (>3-5 cm) with multiple descriptors. On the other hand, while the comparison between pT2b (>5-7) by size only and pT2b by multiple descriptors ($p = 0.88$) indicates that these two groups have similar risks, the comparison of pT2b by multiple descriptors with pT3 tumors by single descriptor ($p = 0.03$) indicates that these groups have significantly different risks not supporting upstaging. (Some data not included in table)

SUPPLEMENTAL TABLE 22. Multivariate Survival Analyses of Clinically Staged T2 and T3 Tumors Classified by Single or Multiple T2 and T3 Descriptors.

Multivariate Results		Survival from diagnosis		
Variable	n/N (%)	HR (95% CI)	P-value	
Other histology vs. adeno	1606/3632 (44%)	1.40 (1.18,1.66)	<.001	
Squamous vs. other	1167/3632 (32%)	0.76 (0.64,0.91)	0.003	
Age >= 60 vs. <60	2914/3632 (80%)	1.67 (1.43,1.95)	<.001	
Male vs. female	2538/3632 (70%)	1.52 (1.33,1.75)	<.001	
Americas vs. Asia	288/3632 (8%)	1.14 (0.92,1.41)	0.238	
Europe/Aus vs. Asia	382/3632 (11%)	1.54 (1.27,1.86)	<.001	
>3-5 cm size only vs Single cT2a <=3 cm	2071/3632 (57%)	1.02 (0.81,1.29)	0.880	
>3-5 cm Multiple vs Single cT2a <=3 cm	178/3632 (5%)	1.12 (0.80,1.56)	0.516	
>5-7 cm size only vs Single cT2a <=3 cm	335/3632 (9%)	1.55 (1.17,2.04)	0.002	
>5-7 cm Multiple descriptors vs.Single cT2a <=3 cm	57/3632 (2%)	1.41 (0.89,2.23)	0.141	
cT3 Single descriptor vs.Single cT2a <=3 cm	485/3632 (13%)	1.81 (1.39,2.34)	<.001	
cT3 Multiple descriptors vs.Single cT2a <=3 cm	231/3632 (6%)	2.23 (1.68,2.96)	<.001	

HR- Hazard Ratio, 95% CI- 95% Confidence Interval, P-value from Wald Chi-Square Test in Cox Regression

n/N (%): n=number with descriptor, N=number evaluated, %=percent with descriptor.

Notes: comparison of cT2a (>3-5 cm) by size only and cT2 a by multiple descriptors (p = 0.49) indicates that these groups have similar risks, differing from the analyses on pathologically staged tumors. In addition, comparison of cT2a by multiple descriptors and cT2b (>5-7 cm) by size only (p = 0.03) indicates that these two groups have different risk, also differing from the analyses on pathologically staged tumors. These findings do not support upstaging of cT2a by multiple descriptors. On the other hand, while the comparison of cT2b (>5-7 cm) by size only and cT2b by multiple descriptors (p = 0.67) indicated that these two groups have similar risks, similarly to the analyses of pathologically staged tumors, the comparison of cT2b tumors by multiple descriptors and cT3 by single descriptor (p = 0.25) indicates that these two groups have similar risks, differing from the analyses of pathologically staged tumors and not supporting the upstaging of cT2b tumors by multiple descriptors.