

Supplementary Online Content

Pathak R, Goldberg SB, Canavan M, et al. Association of survival with adjuvant chemotherapy among patients with early-stage non-small cell lung cancer with vs without high-risk clinicopathologic features. *JAMA Oncol*. Published online September 17, 2020. doi:10.1001/jamaoncol.2020.4232

eTable 1. Propensity Score–Adjusted Multivariable Cox Regression Model for Overall Survival in Tumors ≤ 3 cm

eTable 2. Propensity Score–Adjusted Multivariable Cox Regression Model for Overall Survival in Tumors >3 -4 cm

eTable 3. Propensity Score–Adjusted Multivariable Cox Regression Model for Overall Survival in Tumors >4 -5 cm

eTable 4. Propensity Score–Adjusted Multivariable Cox Regression Model for Overall Survival in Tumors >5 -7 cm

eTable 5. Association of High-Risk Features and Survival After Adjuvant Chemotherapy in Different Tumor Size Categories (≤ 3 cm, >3 -4 cm, >4 -5 cm and >5 -7 cm)

eTable 6. Association of High-Risk Features and Survival After Adjuvant Chemotherapy in ≤ 3 cm Tumors After Adjustments for Clinically Significant Interactions

eTable 7. Association of Sublobar Surgery With Survival After Adjuvant Chemotherapy in ≤ 4 cm Cohort According to 1-cm Tumor Size Increments

eTable 8. Association of High-Risk Features and Survival (Measured From the Date of Diagnosis) After Adjuvant Chemotherapy in Different Tumor Size Categories (≤ 3 cm, >3 -4 cm, >4 -5 cm and >5 -7 cm)

This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Propensity Score–Adjusted Multivariable Cox Regression Model for Overall Survival in Tumors ≤3 cm

Variables	Adjusted HR		
	AHR	95% CI	P Value
Treatment			
Observation	1	Ref	
Adjuvant chemotherapy	1.25	1.10-1.41	.001
Age	1.03	1.03-1.03	<.001
Sex			
Male	1	Ref	
Female	0.72	0.69-0.75	<.001
Race			
White	1	Ref	
Non-white	0.88	0.81-0.95	.001
Insurance			
Not insured	1.30	1.07-1.57	.01
Private insurance	1	Ref	
Medicaid	1.54	1.38-1.73	<.001
Medicare	1.14	1.07-1.22	<.001
Other government	1.15	0.90-1.46	.26
Facility type			
Non-academic ^a	1.12	1.06-1.18	<.001
Academic	1	Ref	
Facility location			
Northeast	1	Ref	
Midwest	1.18	1.10-1.27	<.001
South	1.19	1.11-1.27	<.001
West	1.13	1.03-1.24	.01
Area of residence^b			
Rural	0.98	0.84-1.14	.76
Urban	1.06	1.00-1.14	.07
Metropolitan	1	Ref	
Median income			
<38000	1.16	1.06-1.28	.002
38000 to 47999	1.13	1.04-1.22	.004
48000 to 62999	1.10	1.02-1.18	.01
>63000	1	Ref	

	Adjusted HR		
	AHR	95% CI	P Value
Education, %^c			
≥21	1.18	1.06-1.30	.002
13 to 20.9	1.17	1.07-1.27	.002
7 to 12.9	1.13	1.05-1.21	.002
<7	1	Ref	
Year of diagnosis			
2010	1	Ref	
2011	0.96	0.90-1.03	.28
2012	0.89	0.82-0.95	.001
2013	0.90	0.84-0.97	.01
2014	0.86	0.79-0.93	.002
2015	0.83	0.75-0.91	.001
Histology			
Adenocarcinoma	1	Ref	
SCC	1.07	1.02-1.13	.01
Large cell	1.55	1.36-1.77	<.001
Other ^d	1.14	0.98-1.32	.09
Laterality			
Right	1	Ref	
Left	0.97	0.92-1.01	.16
Primary site			
Main bronchus	1.56	0.35-6.91	.56
Upper lobe	1	Ref	
Middle lobe	1.15	1.04-1.28	.01
Lower lobe	1.07	1.01-1.12	.01
Overlapping lesion	1.06	0.76-1.49	.74
Lung, NOS	1.06	0.85-1.32	.60
VPI			
Absent	1	Ref	
Present	1.10	1.01-1.19	.03
LVI			
Absent	1	Ref	
Present	1.41	1.32-1.51	<.001
Grade			
Well differentiated	1	Ref	
Moderately differentiated	1.49	1.37-1.61	<.001
Poorly differentiated or undifferentiated	1.80	1.65-1.96	<.001

Variables	Adjusted HR		
	AHR	95% CI	P Value
Surgical resection			
Sublobar resection	1.42	1.34-1.50	<.001
Lobectomy	1	Ref	
Pneumonectomy	2.04	1.62-2.55	<.001
Charlson-Deyo score			
0	1	Ref	
1	1.21	1.15-1.28	<.001
≥2	1.54	1.45-1.64	<.001

AHR=Adjusted hazard ratio; CI=Confidence interval; Ref=Reference; NOS=Not otherwise specified; VPI=Visceral pleural invasion; LVI=Lymphovascular invasion.

^aIncludes Community Cancer Program, Comprehensive Community Cancer Program, Integrated Network Cancer Program, and other specified types of cancer programs.

^bBased on patient's zip code area.

^cPercent of people in the patient's zip code area with no high-school diploma.

^dNon-small cell not further defined.

eTable 2. Propensity Score–Adjusted Multivariable Cox Regression Model for Overall Survival in Tumors >3-4 cm

Variables	Adjusted HR		
	AHR	95% CI	P Value
Treatment			
Observation	1	Ref	
Adjuvant chemotherapy	0.93	0.81-1.16	.08
Age	1.03	1.02-1.04	<.001
Sex			
Male	1	Ref	
Female	0.76	0.69-0.83	<.001
Race			
White	1	Ref	
Non-white	0.77	0.66-0.90	.001
Insurance			
Not insured	1.13	0.80-1.60	.48
Private insurance	1	Ref	
Medicaid	1.29	1.02-1.63	.03
Medicare	1.08	0.95-1.22	.23
Other government	1.18	0.78-1.78	.43
Facility type			
Non-academic ^a	1.03	0.93-1.14	.56
Academic	1	Ref	
Facility location			
Northeast	1	Ref	
Midwest	1.24	1.07-1.43	.004
South	1.22	1.07-1.40	.003
West	1.28	1.08-1.51	.004
Area of residence^b			
Rural	1.02	0.77-1.35	.92
Urban	1.06	0.94-1.20	.33
Metropolitan	1	Ref	
Median income			
<38000	1.26	1.06-1.51	.01
38000 to 47999	1.13	0.97-1.32	.12
48000 to 62999	1.07	0.93-1.22	.34
>63000	1	Ref	

Variables	Adjusted HR		
	AHR	95% CI	P Value
Education, %^c			
≥21	0.97	0.80-1.17	.72
13 to 20.9	0.94	0.80-1.10	.45
7 to 12.9	0.97	0.85-1.12	.68
<7	1	Ref	
Year of diagnosis			
2010	1	Ref	
2011	0.97	0.85-1.11	.66
2012	0.94	0.82-1.08	.37
2013	0.97	0.84-1.11	.64
2014	0.78	0.66-0.92	.004
2015	0.89	0.74-1.07	.20
Histology			
Adenocarcinoma	1	Ref	
SCC	1.09	0.99-1.20	.06
Large cell	1.53	1.19-1.98	.001
Other ^d	0.98	0.74-1.29	.86
Laterality			
Right	1	Ref	
Left	0.92	0.84-1.01	.08
Primary site			
Main bronchus	0.50	0.13-2.01	.33
Upper lobe	1	Ref	
Middle lobe	1.05	0.85-1.30	.65
Lower lobe	1.03	0.93-1.13	.57
Overlapping lesion	0.88	0.61-1.26	.49
Lung, NOS	0.99	0.70-1.42	.97
VPI			
Absent	1	Ref	
Present	1.15	1.00-1.32	.05
LVI			
Absent	1	Ref	
Present	1.22	1.08-1.38	.001
Grade			
Well differentiated	1	Ref	
Moderately differentiated	1.40	1.17-1.66	.002
Poorly differentiated or undifferentiated	1.57	1.31-1.87	<.001

Variables	Adjusted HR		
	AHR	95% CI	P Value
Surgical resection			
Sublobar resection	1.59	1.39-1.81	<.001
Lobectomy	1	Ref	
Pneumonectomy	1.36	1.02-1.81	.04
Charlson-Deyo score			
0	1	Ref	
1	1.17	1.06-1.29	.003
≥2	1.32	1.17-1.49	<.001

AHR=Adjusted hazard ratio; CI=Confidence interval; Ref=Reference; NOS=Not otherwise specified; VPI=Visceral pleural invasion; LVI=Lymphovascular invasion.

^aIncludes Community Cancer Program, Comprehensive Community Cancer Program, Integrated Network Cancer Program, and other specified types of cancer programs.

^bBased on patient's zip code area.

^cPercent of people in the patient's zip code area with no high-school diploma.

^dNon-small cell not further defined.

eTable 3. Propensity Score–Adjusted Multivariable Cox Regression Model for Overall Survival in Tumors >4-5 cm

Variables	Adjusted HR		
	AHR	95% CI	P Value
Treatment			
Observation	1	Ref	
Adjuvant chemotherapy	0.75	0.65-0.87	.003
Age	1.03	1.02-1.03	<.001
Sex			
Male	1	Ref	
Female	0.76	0.67-0.86	<.001
Race			
White	1	Ref	
Non-white	0.96	0.79-1.17	.69
Insurance			
Not insured	1.56	1.04-2.32	.03
Private insurance	1	Ref	
Medicaid	1.01	0.72-1.41	.97
Medicare	1.06	0.90-1.26	.48
Other government	1.10	0.63-1.92	.74
Facility type			
Non-academic ^a	1.10	0.96-1.26	.16
Academic	1	Ref	
Facility location			
Northeast	1	Ref	
Midwest	1.32	1.10-1.59	.003
South	1.18	0.98-1.41	.08
West	0.97	0.76-1.23	.81
Area of residence^b			
Rural	1.14	0.79-1.66	.48
Urban	1.04	0.88-1.24	.64
Metropolitan	1	Ref	
Median income			
<38000	0.95	0.74-1.21	.65
38000 to 47999	0.91	0.74-1.11	.35
48000 to 62999	0.91	0.76-1.08	.28
>63000	1	Ref	

Variables	Adjusted HR		
	AHR	95% CI	P Value
Education, %^c			
≥21	1.06	0.81-1.38	.66
13 to 20.9	1.11	0.89-1.37	.36
7 to 12.9	1.08	0.90-1.30	.39
<7	1	Ref	
Year of diagnosis			
2010	1	Ref	
2011	1.11	0.92-1.34	.26
2012	0.96	0.79-1.17	.70
2013	1.14	0.94-1.39	.18
2014	1.03	0.83-1.28	.80
2015	1.13	0.90-1.44	.29
Histology			
Adenocarcinoma	1	Ref	
SCC	1.08	0.95-1.23	.25
Large cell	1.81	1.34-2.44	.004
Other ^d	1.11	0.76-1.62	.60
Laterality			
Right	1	Ref	
Left	1.00	0.88-1.13	.96
Primary site			
Main bronchus	0.83	0.36-1.90	.66
Upper lobe	1	Ref	
Middle lobe	1.31	0.99-1.73	.06
Lower lobe	1.01	0.89-1.14	.91
Overlapping lesion	1.36	0.87-2.11	.18
Lung, NOS	0.89	0.50-1.58	.70
VPI			
Absent	1	Ref	
Present	1.33	1.12-1.59	.001
LVI			
Absent	1	Ref	
Present	1.24	1.06-1.45	.01
Grade			
Well differentiated	1	Ref	
Moderately differentiated	1.48	1.14-1.91	.003
Poorly differentiated or undifferentiated	1.62	1.25-2.10	.002

Variables	Adjusted HR		
	AHR	95% CI	P Value
Surgical resection			
Sublobar resection	1.71	1.38-2.13	<.001
Lobectomy	1	Ref	
Pneumonectomy	1.19	0.88-1.61	.27
Charlson-Deyo score			
0	1	Ref	
1	1.06	0.93-1.22	.38
≥2	1.52	1.30-1.78	<.001

AHR=Adjusted hazard ratio; CI=Confidence interval; Ref=Reference; NOS=Not otherwise specified; VPI=Visceral pleural invasion; LVI=Lymphovascular invasion.

^aIncludes Community Cancer Program, Comprehensive Community Cancer Program, Integrated Network Cancer Program, and other specified types of cancer programs.

^bBased on patient's zip code area.

^cPercent of people in the patient's zip code area with no high-school diploma.

^dNon-small cell not further defined.

eTable 4. Propensity Score–Adjusted Multivariable Cox Regression Model for Overall Survival in Tumors >5-7 cm

Variables	Adjusted HR		
	AHR	95% CI	P Value
Treatment			
Observation	1	Ref	
Adjuvant chemotherapy	0.61	0.54-0.70	<.001
Age	1.03	1.02-1.04	<.001
Sex			
Male	1	Ref	
Female	0.89	0.78-1.01	.062
Race			
White	1	Ref	
Non-white	1.01	0.83-1.24	.90
Insurance			
Not insured	0.90	0.56-1.46	.68
Private insurance	1	Ref	
Medicaid	1.09	0.81-1.47	.57
Medicare	0.86	0.73-1.01	.07
Other government	1.20	0.67-2.14	.55
Facility type			
Non-academic ^a	0.99	0.87-1.14	.93
Academic	1	Ref	
Facility location			
Northeast	1	Ref	
Midwest	1.24	1.02-1.51	.03
South	1.14	0.95-1.37	.16
West	1.12	0.89-1.42	.34
Area of residence^b			
Rural	0.95	0.62-1.44	.80
Urban	0.98	0.82-1.17	.84
Metropolitan	1	Ref	
Median income			
<38000	1.05	0.82-1.36	.69
38000 to 47999	1.09	0.88-1.34	.42
48000 to 62999	1.08	0.90-1.30	.42
>63000	1	Ref	

Variables	Adjusted HR		
	AHR	95% CI	P Value
Education, %^c			
≥21	0.90	0.69-1.18	.46
13 to 20.9	1.02	0.82-1.27	.86
7 to 12.9	1.01	0.84-1.23	.90
<7	1	Ref	
Year of diagnosis			
2010	1	Ref	
2011	0.86	0.71-1.05	.14
2012	0.88	0.72-1.07	.20
2013	0.84	0.69-1.04	.11
2014	1.02	0.83-1.26	.85
2015	0.97	0.76-1.23	.78
Histology			
Adenocarcinoma	1	Ref	
SCC	1.06	0.92-1.21	.44
Large cell	1.02	0.71-1.48	.90
Other ^d	0.81	0.56-1.18	.27
Laterality			
Right	1	Ref	
Left	0.82	0.72-0.94	.003
Primary site			
Main bronchus	3.41	1.28-9.13	.01
Upper lobe	1	Ref	
Middle lobe	1.07	0.77-1.48	.67
Lower lobe	1.20	1.06-1.37	.01
Overlapping lesion	1.15	0.80-1.64	.45
Lung, NOS	1.68	1.08-2.61	.02
VPI			
Absent	1	Ref	
Present	1.23	1.03-1.48	.03
LVI			
Absent	1	Ref	
Present	1.39	1.18-1.64	.004
Grade			
Well differentiated	1	Ref	
Moderately differentiated	1.28	0.99-1.67	.06
Poorly differentiated or undifferentiated	1.46	1.12-1.89	.005

Variables	Adjusted HR		
	AHR	95% CI	P Value
Surgical resection			
Sublobar resection	1.27	0.90-1.79	.18
Lobectomy	1	Ref	
Pneumonectomy	1.31	1.01-1.68	.04
Charlson-Deyo score			
0	1	Ref	
1	1.07	0.93-1.23	.34
≥2	1.39	1.18-1.64	<.001

AHR=Adjusted hazard ratio; CI=Confidence interval; Ref=Reference; NOS=Not otherwise specified; VPI=Visceral pleural invasion; LVI=Lymphovascular invasion.

^aIncludes Community Cancer Program, Comprehensive Community Cancer Program, Integrated Network Cancer Program, and other specified types of cancer programs.

^bBased on patient's zip code area.

^cPercent of people in the patient's zip code area with no high-school diploma.

^dNon-small cell not further defined.

eTable 5. Association of High-Risk Features and Survival After Adjuvant Chemotherapy in Different Tumor Size Categories (≤ 3 cm, >3 -4 cm, >4 -5 cm and >5 -7 cm)

“Overall” refers to all comers in the size category irrespective of high-risk features. LVI indicates lymphovascular invasion; VPI, visceral pleural invasion; high-grade, poor differentiation or undifferentiated.

Features	Total	Adjuvant chemotherapy, No. (%)	HR		
			HR	95% CI	P Value
≤ 3 cm					
Overall	36220	1044 (2.88)	1.10	0.96-1.26	.17
LVI	3508	229 (6.53)	0.88	0.66-1.16	.35
VPI	2813	297 (10.56)	0.90	0.72-1.14	.38
High-grade	10402	465 (4.47)	1.02	0.84-1.25	.81
≥ 2 risk factors ^a	2598	247 (9.51)	0.92	0.76-1.11	.40
Sublobar resection ^b	10891	439 (4.03)	1.07	0.85-1.33	.53
>3-4 cm					
Overall	7501	896 (11.95)	0.90	0.78-1.03	.21
LVI	986	174 (17.65)	0.82	0.60-1.11	.21
VPI	779	123 (15.79)	0.76	0.51-1.12	.22
High-grade	2954	488 (16.52)	1.04	0.86-1.25	.64
≥ 2 risk factors ^a	835	163 (19.52)	0.96	0.73-1.26	.23
Sublobar resection ^b	1172	145 (12.37)	0.72	0.56-0.93	.004
>4-5 cm					
Overall	3711	935 (25.20)	0.75	0.64-0.86	<.001
LVI	537	152 (28.31)	0.62	0.42-0.91	.005
VPI	413	119 (28.81)	0.50	0.32-0.79	<.001
High-grade	1644	492 (29.93)	0.58	0.47-0.72	<.001
≥ 1 risk factor ^a	2057	596 (28.97)	0.67	0.56-0.80	.02
0 risk factor ^a	1654	339 (20.50)	1.06	0.81-1.40	.37
>5 cm					
Overall	3949	1345 (34.06)	0.69	0.62-0.78	<.001
LVI	684	303 (44.30)	0.46	0.34-0.62	<.001
VPI	573	255 (44.50)	0.60	0.43-0.85	.004
High-grade	2253	1002 (44.47)	0.64	0.55-0.75	<.001
0 risk factor ^a	1940	769 (39.64)	0.75	0.61-0.91	.004

^aVPI, LVI or high-grade histology.

^bIn the extended (2004-2015) cohort.

eTable 6. Association of High-Risk Features and Survival After Adjuvant Chemotherapy in ≤ 3 cm Tumors After Adjustments for Clinically Significant Interactions

“Overall” refers to all comers in the size category irrespective of high-risk features. LVI indicates lymphovascular invasion; VPI, visceral pleural invasion; high-grade, poor differentiation or undifferentiated.

Features	HR		
	HR	95% CI	<i>P</i> Value
≤ 3 cm			
Overall	1.54	1.31-1.82	<.001
LVI	0.91	0.69-1.21	.52
VPI	0.78	0.57-1.07	.12
High-grade	1.16	0.96-1.41	.12
≥ 2 risk factors ^a	0.63	0.25-1.61	.33
Sublobar resection ^b	1.18	0.98-1.41	.077

^aVPI, LVI or high-grade histology.

^bIn the extended (2004-2015) cohort.

eTable 7. Association of Sublobar Surgery With Survival After Adjuvant Chemotherapy in ≤ 4 cm Cohort According to 1-cm Tumor Size Increments

Tumor size	Total	Adjuvant chemotherapy, No. (%)	HR		
			HR	95% CI	<i>P</i> Value
0.1-1 cm	1630	51 (3.13)	1.38	0.87-2.20	.07
1.1-2 cm	6098	210 (3.44)	1.14	0.91-1.45	.59
2.1-3 cm	3122	168 (5.38)	1.13	0.88-1.44	.53
3.1-4 cm	1172	145 (12.37)	0.72	0.56-0.93	.004

eTable 8. Association of High-Risk Features and Survival (Measured From the Date of Diagnosis) After Adjuvant Chemotherapy in Different Tumor Size Categories (≤ 3 cm, $>3-4$ cm, $>4-5$ cm and $>5-7$ cm)

“Overall” refers to all comers in the size category irrespective of high-risk features. LVI indicates lymphovascular invasion; VPI, visceral pleural invasion; high-grade, poor differentiation or undifferentiated.

Features	HR		
	HR	95% CI	P Value
≤ 3 cm			
Overall	0.99	0.83-1.19	.94
LVI	0.83	0.59-1.16	.27
VPI	0.71	0.51-1.21	.59
High-grade	0.99	0.76-1.29	.94
≥ 2 risk factors ^a	0.81	0.75-1.11	.32
Sublobar resection ^b	1.04	0.63-1.28	.71
$>3-4$ cm			
Overall	0.83	0.69-1.01	.06
LVI	0.75	0.50-1.12	.16
VPI	0.82	0.50-1.33	.41
High-grade	0.86	0.67-1.12	.24
≥ 2 risk factors ^a	0.93	0.84-1.02	.13
Sublobar resection ^b	0.68	0.54-0.89	.003
$>4-5$ cm			
Overall	0.79	0.66-0.96	.01
LVI	0.55	0.35-0.86	.009
VPI	0.37	0.21-0.64	.004
High-grade	0.72	0.56-0.94	.01
≥ 1 risk factor ^a	0.75	0.70-0.81	<.001
0 risk factor ^a	0.98	0.89-1.07	.59
>5 cm			
Overall	0.61	0.51-0.73	<.001
LVI	0.31	0.19-0.51	<.001
VPI	0.84	0.53-0.89	.005
High-grade	0.57	0.45-0.74	<.001
0 risk factor ^a	0.72	0.66-0.78	<.001

^aVPI, LVI or high-grade histology.

^bIn the extended (2004-2015) cohort.