



Surgery Versus Chemotherapy and Radiotherapy For Early and Locally Advanced Small Cell Lung Cancer: A Propensity-Matched Analysis of Survival

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ABSTRACT

Background: The role of surgery in small cell lung cancer (SCLC) is controversial. Survival outcomes for resection of stage I–IIIA SCLC compared to chemotherapy-based non-surgical treatment (NST) were examined using propensity matching.

Methods: 29,994 clinical stage I–IIIA SCLC patients, including 2,619 undergoing surgery, were identified in the National Cancer Database. Stage-specific propensity scores for receipt of surgery were created. Resected patients were matched 1:1 to those undergoing NST. Overall survival (OS) was assessed using Kaplan–Meier and multivariable Cox models. A separate match was performed comparing Stage I/II patients aged < 85 with a Charlson score of 0 who underwent lobectomy with adjuvant chemotherapy (and radiotherapy if node positive) to those treated with multiagent chemotherapy and concurrent chest radiotherapy (CRT) of at least 40 gray.

Results: 2,089 patients were matched, and cohorts were well balanced. Surgery was associated with longer survival for Stage I (median OS 38.6 months vs. 22.9 months, HR 0.62 95%CI 0.57–0.69, $p < 0.0001$), but survival differences were attenuated for Stage II (median OS 23.4 months vs. 20.7 months, HR 0.84 95%CI 0.70–1.01, $p = 0.06$) and IIIA (median OS 21.7 vs. 16.0 months, HR 0.71 95%CI 0.60–0.83, $p < 0.0001$). In analyses by T and N stage, longer OS was observed in resected patients with stage T3/T4 N0 (median OS 33.0 vs. 16.8 months, $p = 0.008$) and node positivity (N1 + 24.4 vs. 18.3 months $p = 0.03$; N2 + 20.1 vs. 14.6 months $p = 0.007$). In the subgroup analysis, 507 stage I/II patients receiving lobectomy and adjuvant chemotherapy were matched to patients receiving concurrent CRT. In this cohort, lobectomy with adjuvant chemotherapy was associated with significantly longer survival (median OS 48.6 vs. 28.7 months, $p < 0.0001$).

Conclusions: Surgical resection is associated with significantly longer survival for early SCLC. New randomized trials should assess trimodality therapy in stages I/II, and in node negative disease.

1. Introduction

Small cell lung cancer (SCLC) is an aggressive malignancy comprising approximately 15% of new lung cancer diagnoses in the United States and is associated with poor prognosis, even in early stage disease.

[1] The American Cancer Society estimates that 5-year survival for Stage I is 31%, and 19% for Stage II. [2] Given the predisposition for distant metastasis, the standard of care is considered multiagent chemotherapy accompanied by concurrent thoracic radiotherapy and prophylactic cranial irradiation where feasible. [3,4]

Abbreviations: NST, Non-surgical treatment refers to the group receiving chemotherapy with or without radiotherapy; OS, Overall survival; SCLC, Small cell lung cancer; NCDB, National Cancer Database; Gy, Gray

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Table 1

Basic demographic and clinical characteristics of the matched cohorts. Variables included in the propensity score are displayed in the left hand column. *Education level: defined as the percentage of residents in a ZIP code who did not graduate high school (HS).

Variable	All Patients			Stage I			Stage II			Stage IIIA		
	Resected (n = 2,089)	NST (n = 2,089)	P value	Resected (n = 1,310)	NST (n = 1,310)	P value	Resected (n = 335)	NST (n = 335)	P value	Resected (n = 401)	NST (n = 401)	P value
Age, median [IQR]	68[61-74]	68 [61-74]	0.46	68 [62-74]	69 [62-75]	0.23	67 [59 - 74]	67 [60 – 74]	0.54	67 [60 – 73]	66 [57 – 72]	0.21
Male, n (%)	947 (45.3)	955 (45.7)	0.8	570 (43.5)	559 (42.7)	0.66	167 (49.9)	167 (49.9)	1	204 (50.9)	197 (49.1)	0.89
Race, n (%)			0.73			0.75			0.68			0.64
Asian	25 (1.2)	25 (1.2)		16 (1.2)	10 (0.8)		6 (1.8)	9 (2.7)		4 (1.0)	5 (1.3)	
Black	140 (6.7)	134 (6.4)		86 (6.6)	79 (6.0)		23 (6.9)	15 (4.5)		27 (6.7)	32 (8.0)	
Other	6 (0.3)	8 (0.4)		4 (0.3)	4 (0.3)		1 (0.3)	1 (0.3)		1 (0.3)	0 (0.0)	
Unknown	19 (0.9)	12 (0.6)		11 (0.8)	13 (1.0)		1 (0.3)	1 (0.3)		6 (1.5)	3 (0.7)	
White	1,899 (90.1)	1,910 (91.4)		1,193 (91.1)	1,204 (91.9)		304 (90.7)	309 (92.2)		363 (90.5)	361 (90.0)	
Hispanic origin, n (%)			0.88			0.82			0.31			0.45
Non-Hispanic	1,896 (90.7)	1,893 (90.6)		1,192 (90.1)	1,185 (90.5)		310 (92.5)	316 (94.3)		355 (88.5)	343 (85.5)	
Hispanic	35 (1.7)	32 (1.5)		26 (1.7)	26 (2.0)		3 (0.9)	5 (1.5)		6 (1.5)	7 (1.7)	
Unknown	158 (7.6)	164 (7.6)		99 (7.3)	99 (7.6)		22 (6.6)	14 (4.2)		40 (10.0)	51 (12.7)	
Median Income, n (%)			0.99			0.99			0.94			0.99
< \$38,000/year	276 (13.2)	285 (13.6)		175 (13.4)	174 (13.3)		46 (13.7)	41 (12.2)		55 (13.7)	53 (13.2)	
\$38,000 - \$47,999/year	411 (19.7)	403 (19.3)		262 (20.0)	261 (19.9)		73 (21.8)	71 (21.2)		74 (18.5)	71 (17.7)	
\$48,000 - \$62,999/year	587 (28.1)	588 (28.1)		346 (28.7)	387 (19.5)		80 (23.9)	83 (24.8)		108 (26.9)	112 (35.7)	
< \$63,000/year	721 (34.5)	723 (34.6)		446 (34.1)	436 (33.3)		118 (35.2)	118 (35.2)		141 (35.2)	143 (35.7)	
Unknown	94 (4.5)	90 (4.3)		51 (3.9)	52 (4.0)		18 (5.4)	22 (6.6)		23 (5.7)	22 (5.5)	
Education level, n (%)*			0.86			0.93			0.86			0.8
> 21% Did Not Finish HS	334 (16.0)	353 (16.9)		212 (16.2)	198 (15.1)		54 (16.1)	50 (14.9)		65 (16.2)	62 (15.5)	
13-20.9% Did Not Finish HS	603 (28.9)	604 (28.9)		385 (29.4)	400 (30.5)		93 (27.8)	83 (24.8)		116 (28.9)	115 (28.7)	
7-12.9% Did Not Finish HS	715 (34.2)	702 (33.6)		442 (33.7)	437 (33.4)		119 (35.5)	125 (37.3)		137 (34.2)	152 (37.9)	
< 7% Did Not Finish HS	385 (18.4)	386 (18.5)		243 (18.5)	247 (18.5)		58 (17.3)	65 (19.4)		70 (17.5)	61 (15.2)	
Unknown	52 (2.5)	44 (2.1)		28 (2.1)	28 (2.1)		11 (3.3)	12 (3.6)		13 (3.2)	11 (2.7)	
Rural, n (%)	52 (2.5)	52 (2.5)	1	35 (2.7)	25 (1.9)	0.8	7 (2.0)	11 (3.4)	0.97	9 (2.3)	6 (1.5)	0.94
Charlson-Deyo Score, n (%)			0.91			0.65			0.59			0.62
0	1,035 (49.5)	1,031 (49.4)		642 (49.0)	665 (50.8)		166 (49.6)	156 (46.6)		211 (52.6)	214 (53.4)	
1	760 (36.4)	754 (36.1)		474 (36.2)	461 (35.2)		127 (37.9)	140 (41.8)		136 (33.9)	142 (35.4)	
≥ 2	294 (14.1)	304 (14.5)		194 (14.8)	184 (14.1)		42 (12.5)	39 (11.6)		54 (13.5)	45 (11.2)	
Year of diagnosis, n (%)			0.83			0.98			0.82			0.91
2004	146 (7.0)	159 (7.6)		104 (7.9)	102 (7.8)		19 (5.7)	24 (7.2)		25 (6.2)	28 (7.0)	
2005	166 (7.9)	194 (93.3)		106 (8.1)	115 (8.8)		27 (8.1)	23 (6.9)		30 (7.5)	35 (8.7)	
2006	177 (8.5)	188 (9.0)		118 (9.0)	130 (9.9)		25 (7.5)	24 (7.2)		32 (8.0)	24 (6.0)	
2007	173 (8.3)	162 (7.7)		113 (8.6)	102 (7.8)		23 (6.9)	16 (4.8)		34 (8.5)	36 (9.0)	
2008	271 (13.0)	261 (12.5)		165 (12.6)	168 (12.8)		27 (8.1)	37 (11.0)		66 (16.5)	61 (15.2)	
2009	300 (14.4)	303 (14.5)		184 (14.1)	190 (14.5)		53 (15.8)	49 (14.6)		60 (15.0)	64 (16.0)	
2010	290 (13.9)	279 (13.4)		175 (13.4)	170 (13.0)		55 (16.4)	56 (16.7)		58 (14.5)	61 (15.2)	
2011	276 (13.2)	267 (12.8)		167 (12.7)	162 (13.4)		52 (15.5)	57 (17.0)		49 (12.2)	54 (13.5)	
2012	290 (13.9)	276 (13.2)		178 (13.6)	171 (13.1)		54 (16.1)	49 (14.6)		47 (11.7)	38 (9.5)	
Histologic Grade			0.94			0.64			0.81			0.93
Well differentiated	20 (1.0)	25 (1.2)		13 (1.0)	7 (0.5)		4 (1.2)	7 (2.1)		4 (1.0)	4 (1.0)	
Moderately differentiated	45 (2.1)	46 (2.2)		26 (2.0)	24 (1.8)		8 (2.4)	5 (1.5)		8 (2.0)	8 (2.0)	
Poorly differentiated	567 (27.1)	571 (27.3)		328 (25.0)	327 (25.0)		88 (26.3)	85 (25.4)		143 (35.7)	155 (38.7)	
Undifferentiated	660 (31.6)	667 (31.9)		418 (31.9)	439 (33.5)		100 (29.9)	101 (30.2)		119 (29.7)	111 (27.7)	
Undetermined	797 (38.1)	780 (37.3)		525 (40.1)	513 (19.2)		135 (40.6)	137 (40.9)		127 (31.7)	123 (30.7)	
Clinical Stage, n (%)			1									
I	1,336 (64.0)	1,336 (64.0)										
II	348 (16.7)	348 (16.7)										
III	405 (19.4)	405 (19.4)										
Insurance, n (%)			0.98			0.76			0.91			0.42
Not Insured	36 (1.7)	34 (1.63)		23 (1.8)	23 (1.8)		6 (1.8)	9 (2.7)		7 (1.8)	4 (1.0)	
Private Ins.	625 (29.9)	642 (30.7)		359 (27.4)	357 (27.3)		99 (29.6)	95 (28.4)		148 (36.9)	165 (41.1)	
Medicaid	87 (4.2)	83 (4.0)		54 (4.1)	59 (4.5)		16 (4.8)	12 (2.6)		16 (4.0)	15 (3.7)	
Medicare	1,297 (62.1)	1,282 (61.4)		849 (64.8)	453 (65.1)		199 (59.4)	206 (61.5)		224 (55.9)	214 (53.4)	

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