

Prediction of the Risk of Recurrence in Patients with Non-Small Cell Lung Cancer Using an Integrated Claims and Electronic Medical Record Database

ESMO 2022
September 9-13, 2022
Paris, France

Thomas Delea,¹ Aaron Moynahan,¹ Ze Cong,² Karen Chung²
¹PAI, Chestnut Hill, MA, USA; ²GRAIL LLC, a subsidiary of Illumina, Inc.*, Menlo Park, CA, USA

INTRODUCTION

- Lung cancer is the second most common cancer and the most common cause of cancer death in the world¹
- Non-small cell lung cancer (NSCLC) accounts for 84% of all lung cancers²
- Approximately 45% of NSCLC patients are diagnosed with early-stage disease (stage I-II)³
- These patients are typically treated with complete surgical resection of the tumor
- However, 30–55% of such patients will experience recurrence ≤ 5 years after surgery⁴
- Early identification of patients who are at greatest risk of recurrence may permit targeting of adjuvant treatment to those patients most likely to benefit

METHODS

- This was a retrospective observational study to identify predictors of recurrence following resected early-stage NSCLC
- Data were from Optum's de-identified Integrated Claims-Clinical, Enriched Oncology dataset, which contains de-identified, linked enrollment, health insurance claims, and information from electronic medical records (EMR) for enrolled cancer patients from January 1, 2007 to June 30, 2020
- The study sample included patients who had evidence of stage I or II NSCLC, underwent surgical resection after diagnosis of NSCLC, and had ≥ 6 months of enrollment or activity prior to first evidence of lung cancer. Patients with evidence of recurrence before the first surgical resection following NSCLC diagnosis were excluded
- Patient characteristics were assessed as of the date of first surgery following NSCLC diagnosis ("index date") and included age, sex, race, region, insurance type, stage, grade, type of surgery, smoking history, mutation status (EGFR, KRAS, ALK, PDL1), and comorbidities
- Outcomes included recurrence-free survival (RFS), time to recurrence (TTR, with death as censoring event), and overall survival (OS)
- The association between patient characteristics and outcomes were assessed using logistic regression models adjusting for duration of follow-up
- Regressions were alternately conducted using all covariates, and with covariate selection ($p > 0.9$; > 0.10)

KEY RESULTS: IT IS INFEASIBLE TO RELIABLY PREDICT THE RECURRENCE OF EARLY STAGE NSCLC AFTER SURGERY USING INFORMATION FROM A COMMERCIALLY-AVAILABLE LINKED CLAIMS AND EMR DATABASE

Table 1. Patient Attrition

Inclusion Criteria	Patients Remaining
Lung neoplasm identified in histology database	192,002
Non-small cell histology	58,990
Staging information available	38,547
Stage 1 or 2	11,524
Surgery procedure (claims or EHR)	4,235
Lung cancer diagnosis before surgical resection	4,235
≥ 180 days activity prior to lung cancer diagnosis	3,406
No lung cancer recurrence before index date	3,267

Patient Attrition

- Approximately 192,000 patients had lung neoplasm identified in the histology dataset
- A total of 3267 patients met all inclusion criteria

Patient Characteristics

- Mean (SD) age was 67 (9) years; 46% were male
- 27% were current smokers and 67% had stage I disease
- 65.1% of patients underwent lobectomy, 19.2% wedge resection, 3% pneumonectomy, and 12.7% other surgical resection
- KRAS, EGFR, ALK, and PDL1 status were unavailable for 93.5%, 84.1%, 97.2%, and 90.7% of patients respectively; tumor grade was missing for 86% of patients
- Mean (SD) follow-up from index date was 31.0 (23.3) months
- Out of 3267 patients, 722 experienced recurrence, 715 died, and 1134 experienced recurrence or death during follow-up
- Predictors of Recurrence**
 - Results of logistic regressions on RFS, TTR, and OS are shown in **Table 3**
 - Significant predictors of RFS were age, gender, insurance type (Medicaid, Medicare), smoking status (never vs. current), KRAS+, PDL1+, stage (2 vs 1), grade, history of COPD, severe renal disease and HIV
 - Predictors of TTR and OS were generally similar to those for RFS (**Table 3**)
 - The C-statistic was 64.4 for RFS, 64.5 for TTR, and 67.3 for OS, suggesting relatively poor predictive ability for the regression models
 - C-statistics were similar for models using covariate selection (see Figure 1)

Figure 1. Results of Stepwise Logistic Regression on RFS ($P < 10$): C=63.7

Covariate	OR (95%CI)	OR (95%CI); P-Value
Never smoker (vs. Current)	0.592 (0.45 - 0.78)	.0015
Female (vs. Male)	0.732 (0.65 - 0.83)	.0002
Black (vs. White)	0.813 (0.65 - 1.02)	<.0001
Myocardial infarction (vs. None)	1.206 (0.98 - 1.49)	<.0001
Medicare (vs. Commercial)	1.231 (1.08 - 1.40)	<.0001
Grade Poorly Differentiated/Undifferentiated (vs. Missing)	1.246 (1.01 - 1.54)	.0253
COPD (vs. None)	1.295 (1.15 - 1.46)	.0803
Age ≥ 75 y (vs. < 64 y)	1.297 (1.13 - 1.49)	<.0001
Grade Moderately/Moderately to Poorly differentiated (vs. Missing)	1.351 (1.04 - 1.76)	.0012
Stage 2bc (vs. Stage 1)	1.442 (1.21 - 1.72)	<.0001
Stage 2a (vs. Stage 1)	1.464 (1.21 - 1.77)	<.0001
Stage 2 (vs. Stage 1)	1.613 (1.35 - 1.94)	.0390
KRAS+ (vs. Negative/Unknown/Missing)	1.665 (1.28 - 2.17)	.0001
Medicaid (vs. Commercial)	1.699 (1.31 - 2.20)	.0689
PDL1+ (vs. Negative/Unknown/Missing)	1.778 (1.44 - 2.19)	.0002
Grade Unclassified (vs. Missing)	1.826 (1.27 - 2.63)	<.0001
Severe Renal Disease (vs. None)	2.071 (1.39 - 3.09)	<.0001
HIV (vs. None)	2.166 (1.11 - 4.23)	.0004

Table 2. Patient Characteristics

Characteristic	All Patients (N=3,267)	Patients Experiencing Recurrence (N=722)
Age, y, Mean (SD)	67.3 (9.2)	67.0 (9.4)
Age Group, Count (%)		
0-54 y	274 (8.4%)	74 (10.2%)
55-64 y	982 (30.1%)	199 (27.6%)
65-74 y	1,231 (37.7%)	281 (38.9%)
75-84 y	736 (22.5%)	161 (22.3%)
85+ y	44 (1.3%)	7 (1.0%)
Gender, Count (%)		
Male	1,505 (46.1%)	372 (51.5%)
Female	1,760 (53.9%)	349 (48.3%)
Race, Count (%)		
Black	294 (9.0%)	61 (8.4%)
Asian	39 (1.2%)	6 (0.8%)
White	2,836 (86.8%)	640 (88.6%)
Other/Unknown	98 (3.0%)	15 (2.1%)
Region, Count (%)		
Midwest	1,532 (46.9%)	390 (54.0%)
Northeast	863 (26.4%)	191 (26.5%)
South	493 (15.1%)	75 (10.4%)
West	279 (8.5%)	47 (6.5%)
Other/Unknown	100 (3.1%)	19 (2.6%)
Insurance, Count (%)		
Commercial	1,153 (35.3%)	258 (35.7%)
Medicaid	185 (5.7%)	39 (5.4%)
Medicare Advantage	1,654 (50.6%)	380 (52.6%)
Other Payor	156 (4.8%)	28 (3.9%)
Uninsured	118 (3.6%)	17 (2.4%)
Missing	1 (0.0%)	0 (0.0%)
Smoking Status, Count (%)		
Previous	1,947 (59.6%)	458 (63.4%)
Current	884 (27.1%)	186 (25.8%)
Never	274 (8.4%)	37 (5.1%)
Not current	145 (4.4%)	38 (5.3%)
Other	3 (0.1%)	1 (0.1%)
Missing/Unknown	14 (0.4%)	2 (0.3%)
KRAS, Count (%)		
Positive	118 (3.6%)	58 (8.0%)
Negative	93 (2.8%)	24 (3.3%)
Unknown	1 (0.0%)	0 (0.0%)
Missing	3,055 (93.5%)	640 (88.6%)
EGFR, Count (%)		
Positive	168 (5.1%)	49 (6.8%)
Negative	347 (10.6%)	132 (18.3%)
Unknown	4 (0.1%)	1 (0.1%)
Missing	2,748 (84.1%)	540 (74.8%)
ALK, Count (%)		
Positive	48 (1.5%)	12 (1.7%)
Negative	365 (11.2%)	131 (18.1%)
Unknown	6 (0.2%)	2 (0.3%)
Missing	2,848 (87.2%)	577 (79.9%)
PDL1, Count (%)		
Positive	214 (6.6%)	83 (11.5%)
Negative	86 (2.6%)	25 (3.5%)
Unknown	5 (0.2%)	2 (0.3%)
Missing	2,962 (90.7%)	612 (84.8%)
Tumor Grade, Count (%)		
Missing	2,811 (86.0%)	584 (80.9%)
Well differentiated	49 (1.5%)	13 (1.8%)
Moderately differentiated	118 (3.6%)	37 (5.1%)
Moderately to poorly differentiated	10 (0.3%)	3 (0.4%)
Poorly differentiated	222 (6.8%)	62 (8.6%)
Undifferentiated	4 (0.1%)	1 (0.1%)
Unclassified	53 (1.6%)	22 (3.0%)
Stage, Count (%)		
1	905 (27.7%)	167 (23.1%)
1a	677 (20.7%)	142 (19.7%)
1a1	10 (0.3%)	1 (0.1%)
1a2	85 (2.6%)	7 (1.0%)
1b	525 (16.1%)	120 (16.6%)
1c	1 (0.0%)	0 (0.0%)
2	344 (10.5%)	85 (11.8%)
2a	304 (9.3%)	91 (12.6%)
2b	414 (12.7%)	107 (14.8%)
2c	2 (0.1%)	2 (0.3%)
Months of Follow-up, Mean (SD)	31.0 (23.3)	39.2 (22.5)
Comorbidities, Count (%)		
Myocardial infarction	211 (6.5%)	55 (7.6%)
Congestive heart failure	6 (0.2%)	0 (0.0%)
Cerebrovascular disease	50 (1.5%)	10 (1.4%)
Dementia	45 (1.4%)	11 (1.5%)
COPD	1,594 (48.8%)	393 (54.4%)
Rheumatoid arthritis	23 (0.7%)	9 (1.2%)
Mild liver disease	6 (0.2%)	1 (0.1%)
Severe renal disease	48 (1.5%)	10 (1.4%)
HIV	15 (0.5%)	6 (0.8%)
AIDS	16 (0.5%)	1 (0.1%)
Type of Lung Surgery, Count (%)		
Lobectomy	2,127 (65.1%)	418 (57.9%)
Wedge resection	628 (19.2%)	141 (19.5%)
Pneumonectomy	97 (3.0%)	32 (4.4%)
Other	415 (12.7%)	131 (18.1%)

AIDS, acquired immunodeficiency syndrome; COPD, chronic obstructive pulmonary disease; HIV, human immunodeficiency virus.

Table 3. Result of Logistic Regressions on RFS, TTR, and OS

Covariate	OR (95%CI)		
	RFS	TTR	OS
Intercept	0.01 (0.01-0.01) [§]	0.01 (0.00-0.01) [§]	0.01 (0.00-0.01) [§]
Age Group			
0-64 y	1.00 (-, -)	1.00 (-, -)	1.00 (-, -)
65-74 y	1.07 (0.91-1.27)	1.15 (0.94-1.40)	1.02 (0.82-1.26)
75+ y	1.37 (1.15-1.64) [†]	1.12 (0.89-1.41)	1.64 (1.31-2.06) [§]
Gender			
Male	1.00 (-, -)	1.00 (-, -)	1.00 (-, -)
Female	0.72 (0.64-0.82) [§]	0.76 (0.65-0.88) [†]	0.71 (0.60-0.83) [§]
Race			
White	1.00 (-, -)	1.00 (-, -)	1.00 (-, -)
Black	0.80 (0.64-1.01)	0.89 (0.68-1.16)	0.75 (0.55-1.01)
Asian	0.83 (0.41-1.69)	0.90 (0.39-2.04)	0.57 (0.18-1.81)
Other/Unknown	0.81 (0.54-1.20)	0.71 (0.42-1.19)	1.00 (0.63-1.60)
Region			
Midwest	1.00 (-, -)	1.00 (-, -)	1.00 (-, -)
Northeast	0.87 (0.74-1.01)	0.98 (0.81-1.18)	0.67 (0.54-0.82) [†]
South	0.95 (0.80-1.14)	0.71 (0.55-0.92) [†]	1.19 (0.96-1.47)
West	0.94 (0.74-1.20)	0.92 (0.68-1.26)	0.96 (0.71-1.29)
Other/Unknown	0.69 (0.47-1.01)	0.74 (0.47-1.18)	0.60 (0.36-0.99) [*]
Insurance			
Commercial	1.00 (-, -)	1.00 (-, -)	1.00 (-, -)
Medicaid	1.70 (1.30-2.22) [†]	1.25 (0.88-1.78)	1.91 (1.37-2.66) [†]
Medicare Advantage	1.19 (1.02-1.38) [*]	1.02 (0.85-1.23)	1.31 (1.08-1.60) [†]
Other Payor	1.08 (0.79-1.48)	0.94 (0.63-1.40)	1.17 (0.79-1.73)
Uninsured	0.79 (0.53-1.17)	0.65 (0.39-1.08)	0.80 (0.48-1.35)
Smoking Status			
Current	1.00 (-, -)	1.00 (-, -)	1.00 (-, -)
Previous	0.89 (0.77-1.02)	1.01 (0.85-1.21)	0.91 (0.76-1.08)
Never	0.53 (0.40-0.72) [§]	0.52 (0.36-0.76) [†]	0.66 (0.45-0.96) [*]
Not Current	0.95 (0.70-1.28)	1.20 (0.84-1.72)	0.98 (0.68-1.41)
Other/Missing/Unknown	0.89 (0.41-1.90)	0.74 (0.23-2.32)	0.67 (0.25-1.82)
KRAS			
Negative/Unknown/Missing	1.00 (-, -)	1.00 (-, -)	1.00 (-, -)
Positive	1.66 (1.27-2.17) [†]	2.42 (1.82-3.23) [†]	1.02 (0.70-1.50)
EGFR			
Negative/Unknown/Missing	1.00 (-, -)	1.00 (-, -)	1.00 (-, -)
Positive	1.21 (0.93-1.56)	1.32 (0.97-1.80)	1.07 (0.76-1.51)
ALK			
Negative/Unknown/Missing	1.00 (-, -)	1.00 (-, -)	1.00 (-, -)
Positive	0.93 (0.56-1.54)	0.99 (0.55-1.78)	0.96 (0.51-1.81)
PDL1			
Negative/Unknown/Missing	1.00 (-, -)	1.00 (-, -)	1.00 (-, -)
Positive	1.77 (1.43-2.19) [§]	2.08 (1.63-2.65) [†]	1.37 (1.04-1.81) [*]
Tumor Grade			
Missing	1.00 (-, -)	1.00 (-, -)	1.00 (-, -)
Well differentiated	0.88 (0.55-1.42)	1.11 (0.63-1.94)	0.42 (0.20-0.89) [*]
Moderately/Moderately to poorly differentiated	1.34 (1.03-1.75) [*]	1.42 (1.02-1.97) [*]	1.27 (0.92-1.75)
Poorly/Undifferentiated	1.24 (1.00-1.53) [*]	1.16 (0.89-1.52)	1.25 (0.97-1.61)
Unclassified	1.84 (1.27-2.65) [†]	2.13 (1.38-3.30) [†]	1.49 (0.94-2.35)
Stage, Count (%)			
1	1.00 (-, -)	1.00 (-, -)	1.00 (-, -)
1a	0.93 (0.78-1.12)	1.09 (0.87-1.37)	0.84 (0.67-1.06)
1a1	0.87 (0.21-3.56)	1.00 (0.14-7.22)	1.17 (0.28-4.86)
1a2	0.66 (0.35-1.25)	0.81 (0.38-1.74)	0.70 (0.31-1.58)
1bc	1.07 (0.89-1.30)	1.22 (0.96-1.55)	0.91 (0.71-1.16)
2	1.61 (1.31-1.97) [§]	1.61 (1.23-2.10) [†]	1.47 (1.14-1.88) [†]
2a	1.45 (1.18-1.79) [†]	1.70 (1.31-2.21) [†]	1.34 (1.03-1.73) [*]
2bc	1.43 (1.17-1.74) [†]	1.59 (1.23-2.04) [†]	1.38 (1.07-1.76) [*]
Comorbidities			
Myocardial infarction	1.19 (0.96-1.47)	1.06 (0.80-1.41)	1.28 (0.99-1.64)
Congestive heart failure	0.65 (0.09-4.78)	1.00 (-, -)	1.28 (0.17-9.38)
Cerebrovascular disease	0.78 (0.46-1.32)	0.85 (0.45-1.61)	0.78 (0.41-1.47)
Dementia	1.44 (0.89-2.33)	1.58 (0.86-2.91)	1.68 (0.96-2.96)
COPD	1.25 (1.10-1.41) [†]	1.18 (1.02-1.38) [*]	1.35 (1.15-1.58) [†]
Rheumatoid arthritis	1.37 (0.78-2.40)	1.51 (0.77-2.96)	1.46 (0.77-2.77)
Mild liver disease	1.77 (0.56-5.61)	0.78 (0.11-5.63)	3.68 (1.15-11.74) [*]
Severe renal disease	2.17 (1.45-3.27) [†]	1.41 (0.75-2.68)	2.50 (1.58-3.93) [§]
HIV	2.32 (1.18-4.56) [*]	2.16 (0.95-4.93)	3.05 (1.48-6.30) [†]
AIDS	0.59 (0.19-1.87)	0.29 (0.04-2.09)	0.75 (0.18-3.05)
Type of Lung Surgery			
Lobectomy	1.00 (-, -)	1.00 (-, -)	1.00 (-, -)
Wedge	1.15 (0.98-1.35)	1.19 (0.97-1.45)	1.11 (0.90-1.36)
Pneumonectomy	1.06 (0.77-1.45)	1.24 (0.85-1.80)	1.31 (0.92-1.87)
Other	1.17 (1.00-1.38)	1.21 (0.99-1.48)	1.09 (0.89