

Current Treatment of Lung Comorbidities in Lung Cancer Patients

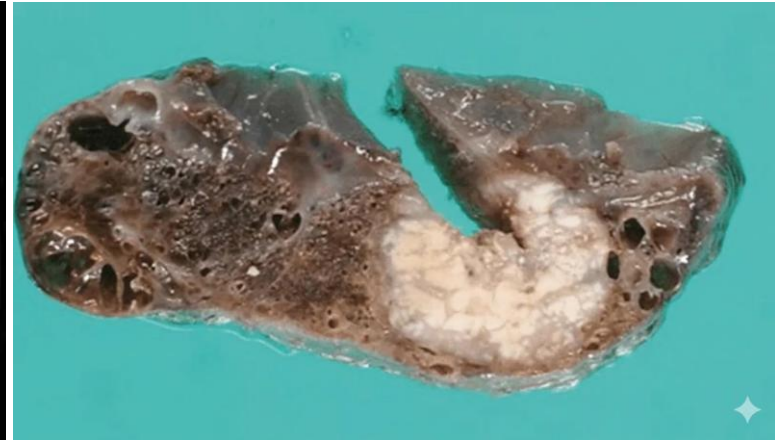
: Evidence-based Strategies for co-existing IPF and COPD

은평성모병원 호흡기내과

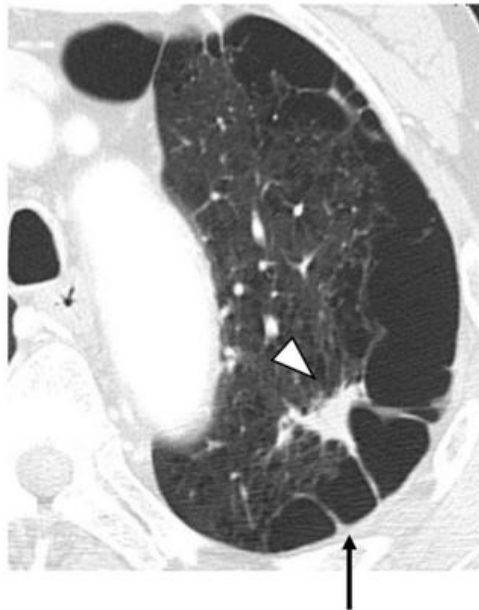
여창동

Today's Contents

- IPF



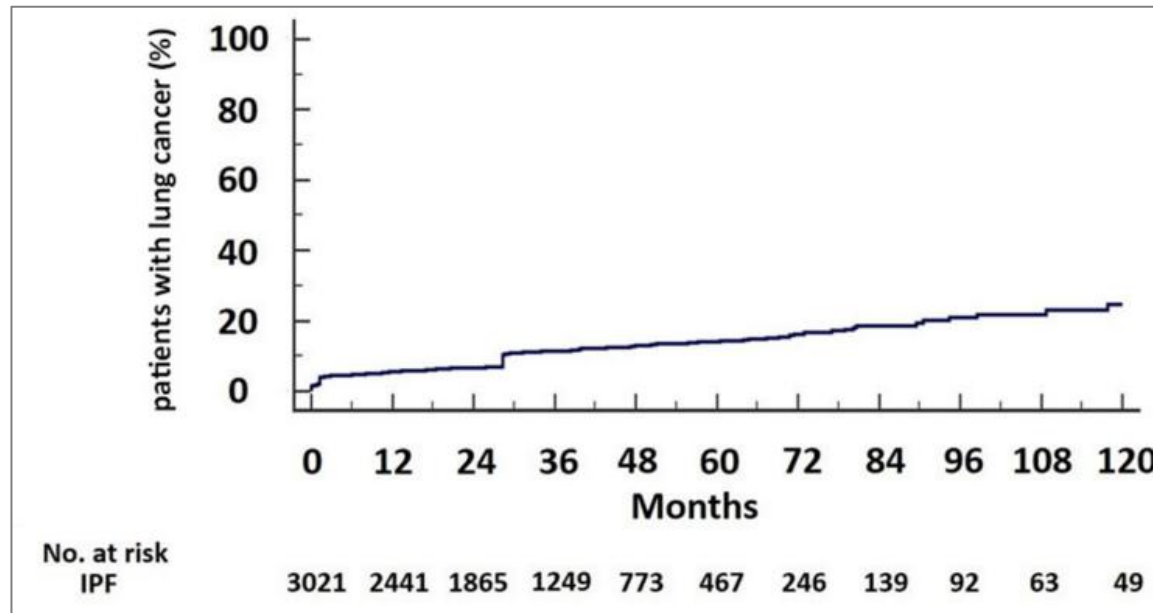
- COPD (emphysema)



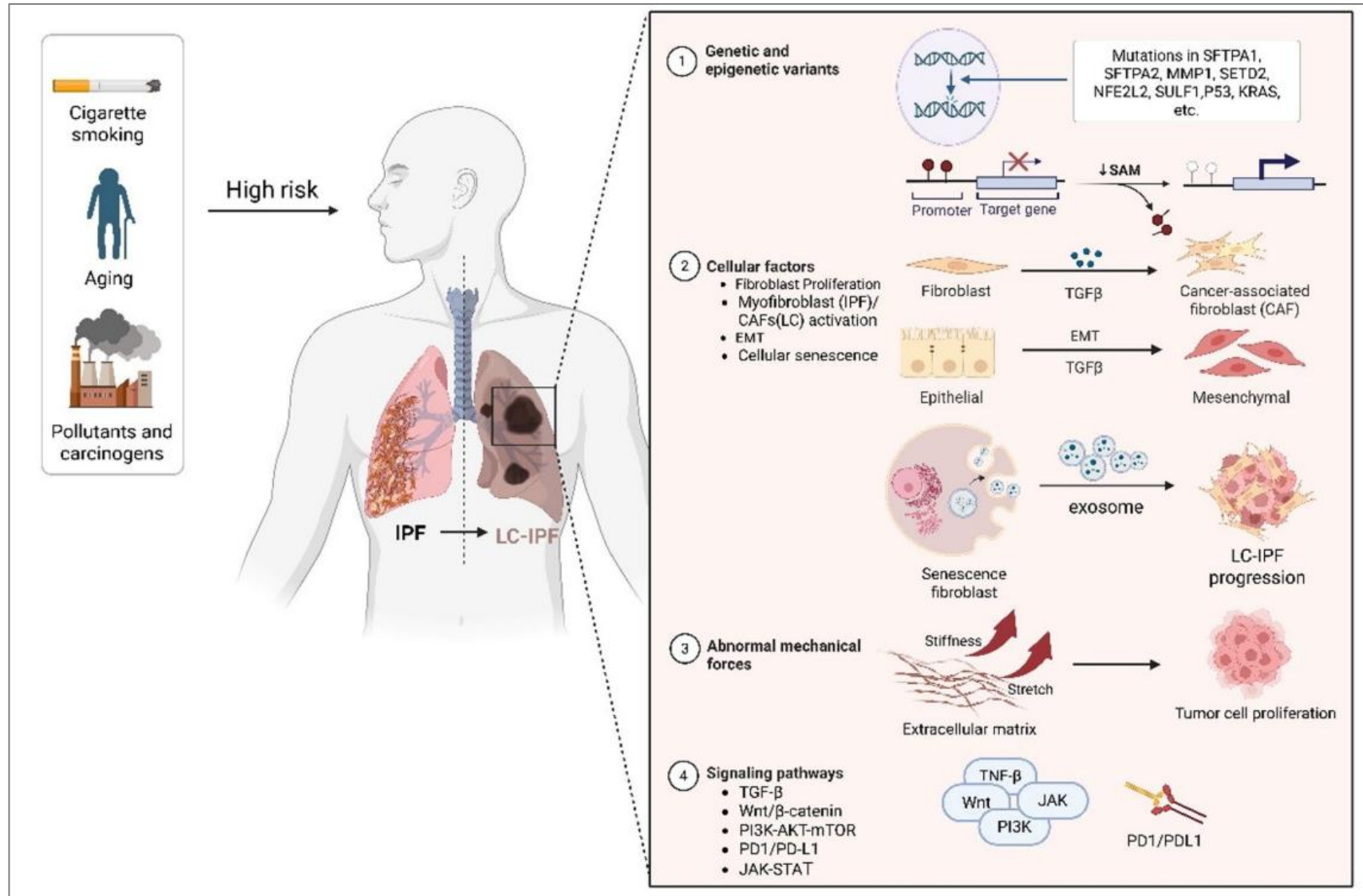
Epidemiology

Table 1 Reported lung cancer incidence rates in patients with pulmonary fibrosis from 2017 to 2023 [12, 15, 17–20]

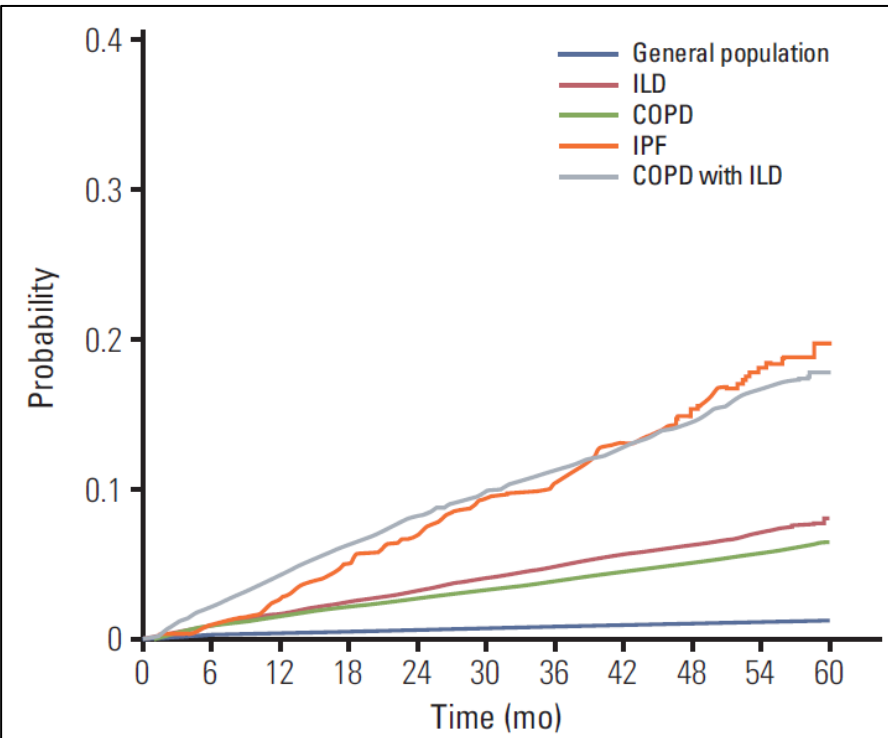
Study	Country	Years	Study design	Cases of IPF (n)	Incidence of lung cancer (%)
Liu et al., 2017	China	2008–2012	Retrospective;	268	17.16%
Yoo et al., 2018	USA	2000–2015	single-center	1108	2.8%
Tzouvelekis et al., 2020	Greece	2011–2018	Retrospective;	1016	10.03%
LEE et al., 2020	Korea	2009–2014	two centers	25,241	15.66%
Song et al., 2021	Korea	2012–2016	Retrospective;	7277	6.4%
Sun et al., 2022	China	2015–2021	eight centers	535	3.9%
Karampitsakos et al., 2023	Europe	2010–2021	Retrospective; multicenter	3178	10.2%
LEE et al., 2023	Korea	2011–2019	Retrospective; multicenter	21,111	3.34%
			Retrospective;		
			single-center		
			Retrospective; multicenter		
			Retrospective; multicenter		



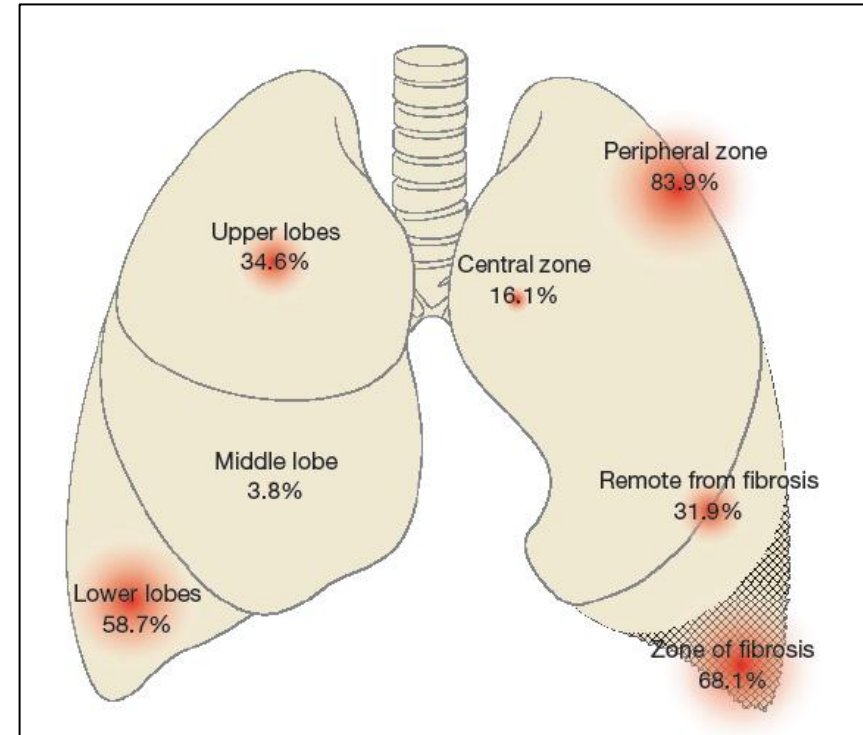
Common Pathogenic Mechanism



Epidemiology



Cancer Res Treat 2018;50(2):374-381

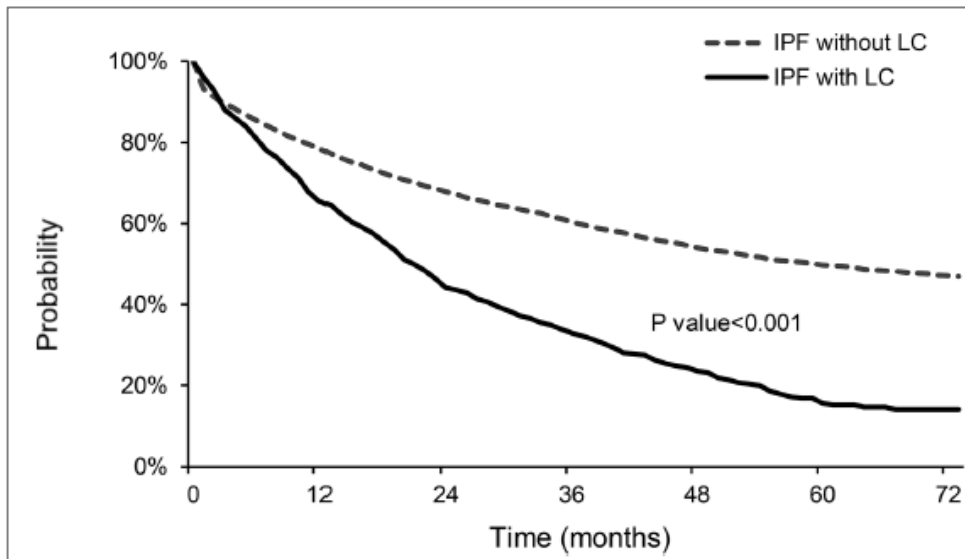


J Thorac Dis 2018;16(6):3829-3844

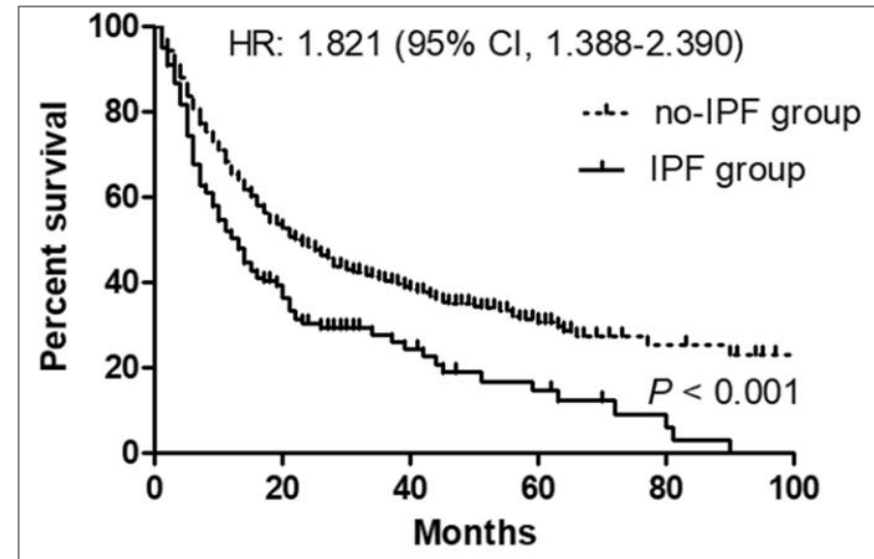
Univariate and multivariate cox regression analysis identifying risk factors for lung cancer development in IPF patients.

Parameters	Univariate analysis <i>P</i> -value	Multivariate analysis <i>P</i> -value
Antifibrotic therapy	.032	.046
Emphysema	.024	.016
Low BMI	.006	.004
≥ 36 pack-yr smoking	.004	.006
Weight loss	.025	.037

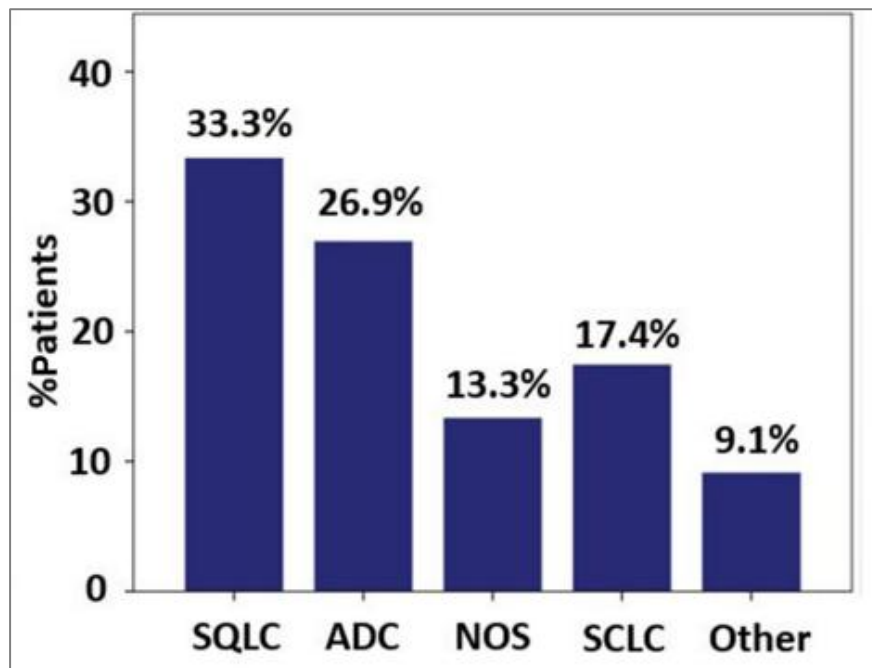
- IPF with/without Lung Cancer



- Lung Cancer with/without IPF



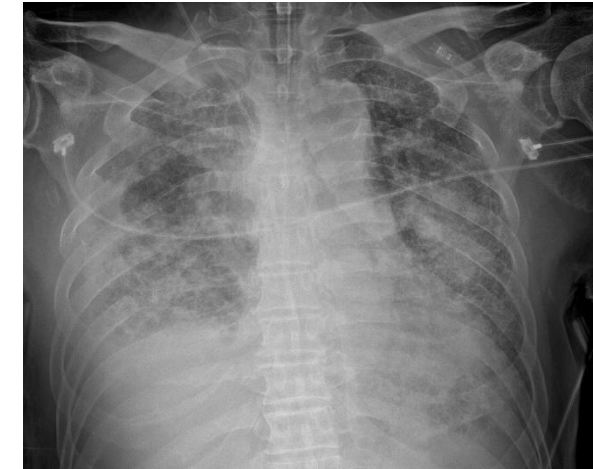
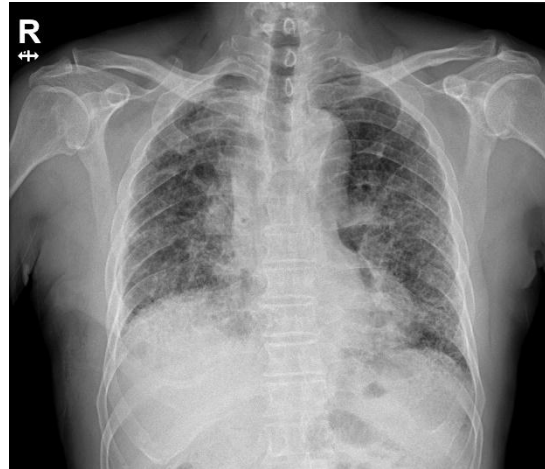
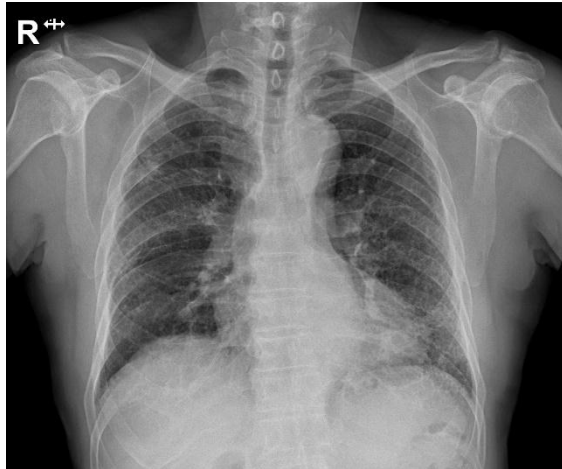
Clinico-pathological characteristics



	IPF Patients <i>n</i> = 43	Non- IPF Patients <i>n</i> = 55	<i>p</i> -Value
mPD-L1	12 (28%)	5 (9%)	0.015
gPD-L1	33 (76%)	48 (89%)	0.172
Fibroblast foci	17 (40%)	13 (24%)	0.09
Honeycombing	9 (21%)	2 (4%)	0.007
Patchy fibrosis	41 (95%)	43 (78%)	0.016
Patchy fibrosis + fibroblast foci	17 (40%)	12 (22%)	0.057

Variables	Non-UIP- ADC	UIP- ADC	<i>p</i> Value
Sex, <i>n</i> (%)			<0.01
Male	1114 (49.2)	41 (93.2)	
Female	1151 (50.8)	3 (6.8)	
Age, <i>y</i>			<0.01
Median	63.8	69	
Range	23–82	52–89	
Smoking, <i>n</i> (%)			<0.01
Never	1215 (53.6)	4 (9.1)	
Former/present	1058 (46.4)	40 (90.9)	
EGFR, <i>n</i> (%)			< 0.01
Wild type	907 (54.4)	42 (97.7)	
Mutation	759 (45.6)	1 (2.3)	
KRAS, <i>n</i> (%)			< 0.01
Wild type	1498 (91.5)	30 (69.8)	
Mutation	139 (8.5)	13 (30.2)	

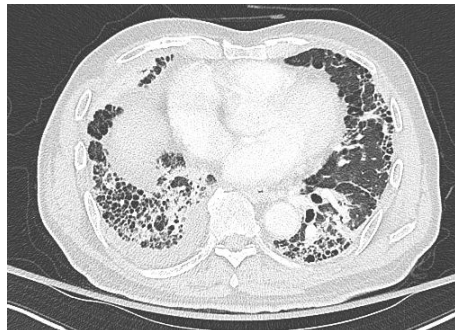
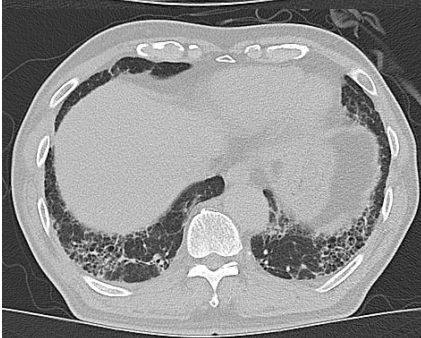
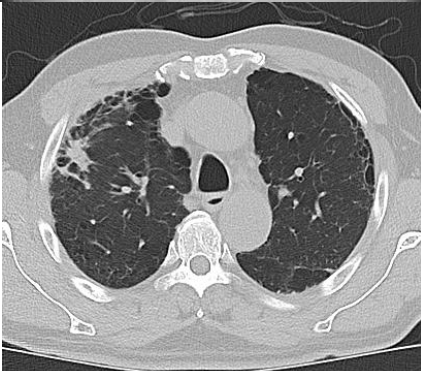
Case #1



POD 3

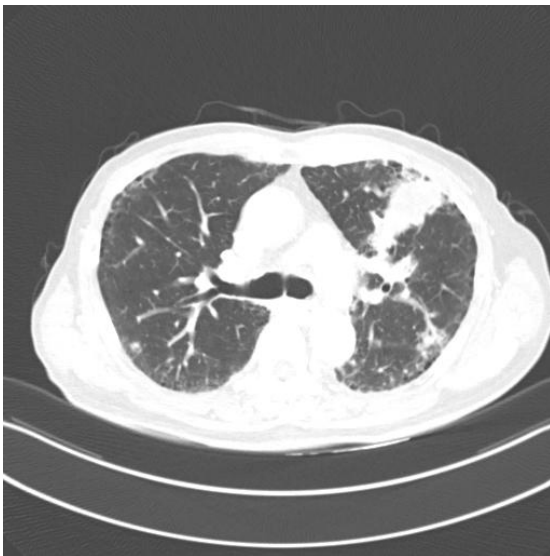
POD 30

- 72/M
- Ex-smoker, 40PY
- ADC, cT1bN0M0
- FVC 80%, DLco 71%
- History of AE (-)



Case #2

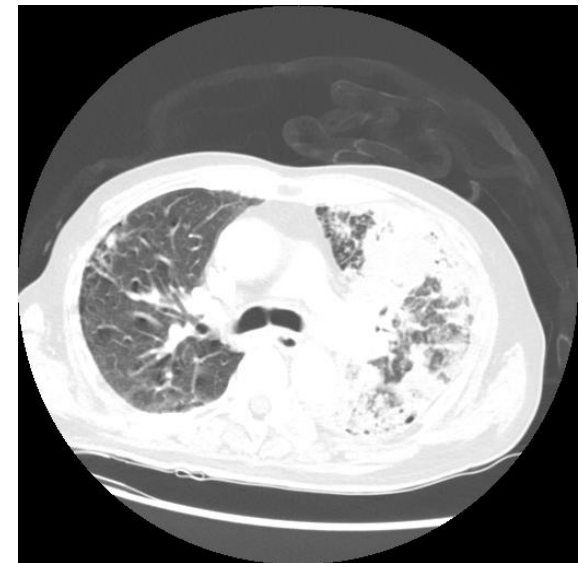
- 72/M
- Current smoker, 50PY
- ADC, cT4N3M1c
- EGFR/ALK (-), PD-L1 60%
- IPF (FVC 75%, DLco 60%)
- PD after 1st line Paclitaxel-carboplatin



2021.6.24



2nd line
atezolizumab



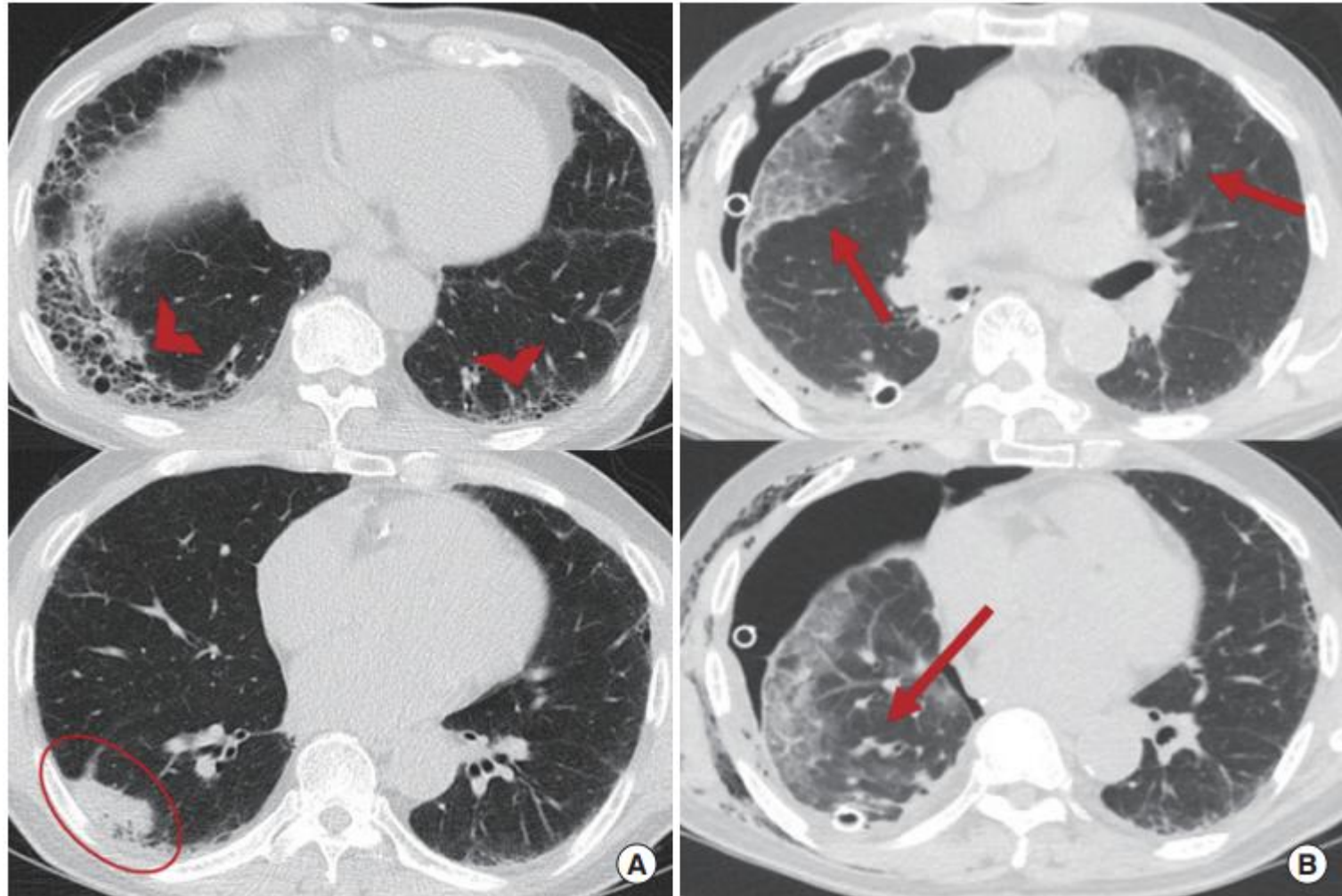
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Proposal for Therapeutic Strategies



Treatment	Stage I-IB	Stage IIA-IIIa	Stage IIIB/C	Stage IV		
Eligibility	Age, PS, FEV ₁ /D _{LCO} , comorbidities			Age, PS, histology, comorbidities, "auto-immunity"		
Biomarkers	NA	NA	NA	Addiction (adenocarcinoma)	PD-L1 ≥50%	PD-L1 <50%
• Specific eligibility criteria for fILD: UIP <i>versus</i> others, CT-scan extension grading, FVC and D_{LCO} evaluation, ILD-GAP index • Consider introduction of an antifibrotic drug						
Standard	Lobectomy VATS No adjuvant chemotherapy		Treat as stage IV?	Carboplatin weekly (nab-)paclitaxel (± bevacizumab)	Carboplatin weekly (nab-)paclitaxel (± bevacizumab)	Carboplatin weekly (nab-)paclitaxel (± bevacizumab)
					Nivolumab/pembrolizumab second line?	
Option/not fit	SBRT Sublobar resection	Treat as stage IV?	Treat as stage IV?	Kinase inhibitors?	Mono-chemotherapy Paclitaxel, vinorelbine, pemetrexed	
Frail/oldest patients/PS2	SBRT	Palliative care	Palliative care	Kinase inhibitor	Palliative care	Palliative care

Postoperative AE of IPF



Risk factors for Postoperative AE of IPF

Table 2. The incidence of AE and mortality due to AE in patients with IPF undergoing LC resection.

Original Articles					
Author	Reference	Published Year	Number of Patients, n	Number of AEs, n (%)	Number of AE Deaths, n (%)
Kanazaki	[163]	2010	40	12 (30)	3 (25)
Park	[164]	2011	100	28 (28)	13 (46.7)
Maniwa	[165]	2013	89	8 (9)	1 (12.5)
Sato	[159]	2014	1763	164 (9.4)	72 (43.9)
Omori	[166]	2015	103	5 (4.90)	3 (60)
Joo	[167]	2016	80	6 (7.5)	NA
Kobayashi	[168]	2016	137	17 (12.4)	7(41.2)
Tsutani	[169]	2017	107	6 (5.6)	NA
Shao	[162]	2019	97	7(6.2)	5 (83.3)
Tang	[170]	2020	156	7 (4.5)	5 (71.4)
Kato	[171]	2023	68	8 (11.8)	1 (12.5)
Fujiwara	[172]	2023	91	14 (15.4)	9 (64)
Meta-analysis					
Hao	[160]	2022	2655	258 (9.7)	NA
Patel	[161]	2023	2202	322 (14.6)	NA

Risk factors for Postoperative AE of IPF

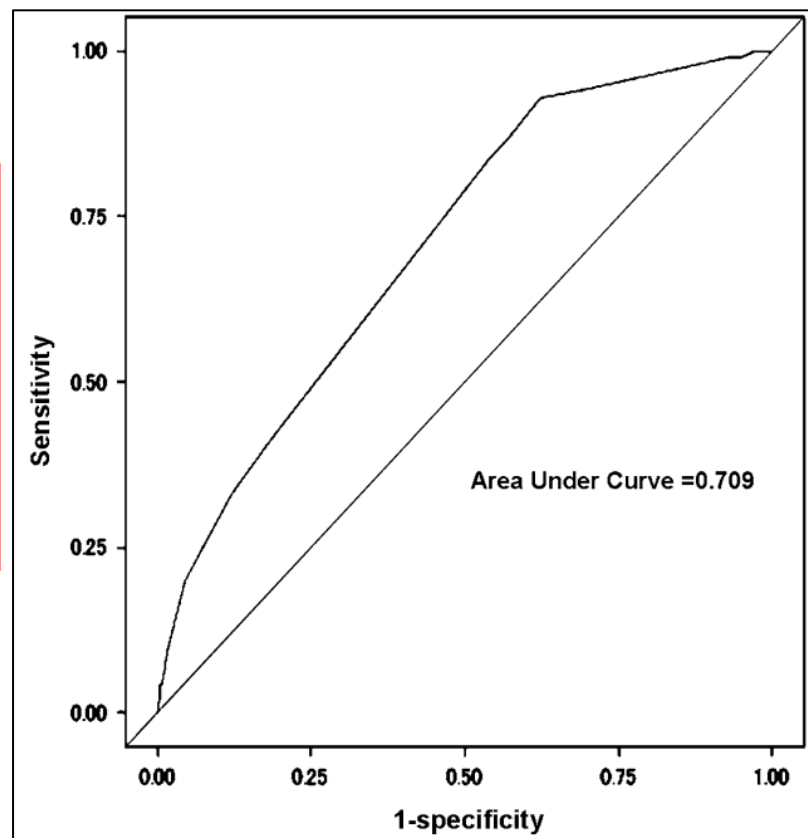
Factors	All patients (n = 1763)					UIP subgroup (n = 1235)*				
	Patients (n)	AE (%)	OR	95% CI	P value	Patients (n)	AE (%)	OR	95% CI	P value
Surgical procedures					.0005†					.0005†
Wedge resection	275	10 (3.6)	1.000	—	—	202	10 (5.0)	1.000	—	—
Lobectomy/segmentectomy	1386	138 (10.0)	3.83	1.941-7.567	.0001	955	100 (10.5)	2.91	1.453-5.847	.0026
Bilobectomy/pneumonectomy	94	15 (16.0)	5.7	2.381-13.66	.0001	70	14 (20.0)	5.96	2.413-14.74	.0001
N/A	8	1 (12.5)				8	1 (12.5)			
KL-6 (U/mL)										
<1000‡	834	68 (8.2)	1.000	—	—	571	56 (9.8)	1.000	—	—
≥1000	209	34 (16.3)	2.14	1.344-3.394	.0013	151	27 (17.9)	2.02	1.199-3.408	.0083
N/A	720	62 (8.6)				513	42 (8.2)			
Sex										
Male	1593	158 (9.9)	1.000	—	—	1138	123 (10.8)	1.000	—	—
Female	170	6 (3.5)	0.3	0.126-0.688	.0047	97	2 (2.1)	0.18	0.043-0.737	.0172
%VC										
<80	263	36 (13.7)	1.000	—	—	191	30 (15.7)	1.000	—	—
≥80	1478	126 (8.5)	0.63	0.417-0.959	.0308	1033	94 (9.1)	0.57	0.350-0.884	.0131
N/A	22	2 (9.1)				11	1 (9.1)			
History of AE										
—	1741	158 (9.1)	1.000	—	—	1223	120 (9.8)	1.000	—	—
+	20	6 (30.0)	3.24	1.063-9.897	.0387	10	5 (50.0)	7.67	1.997-29.42	.0030
N/A	2	0 (0.0)				2	0 (0.0)			
Preoperative steroid use										
—	1651	144 (8.7)	1.000	—	—					
+	103	20 (19.4)	2.46	1.356-4.454	.0031					
N/A	9	0 (0.0)								
CT findings										
UIP pattern	1300	134 (10.3)	1.000	—	—					
Non-UIP pattern	463	30 (6.5)	0.59	0.386-0.900	.0143					

Risk factors for Postoperative AE of IPF

Table 1 Risk scoring system for predicting acute exacerbation of interstitial pneumonia after pulmonary resection in lung cancer patients

History of acute exacerbation	5
CT findings: UIP pattern	4
Surgical procedure > wedge resection	4
Preoperative steroid use	3
Male gender	3
KL-6 > 1,000 U/mL	2
% vital capacity	1

Grade of risk	Risk score
Low risk < 10%	< 11
Intermediate risk < 10–25%	11–14
High risk < 25%	> 14



Risk factors for Postoperative AE of IPF



Impact and predictors of acute exacerbation of interstitial lung diseases after pulmonary resection for lung cancer

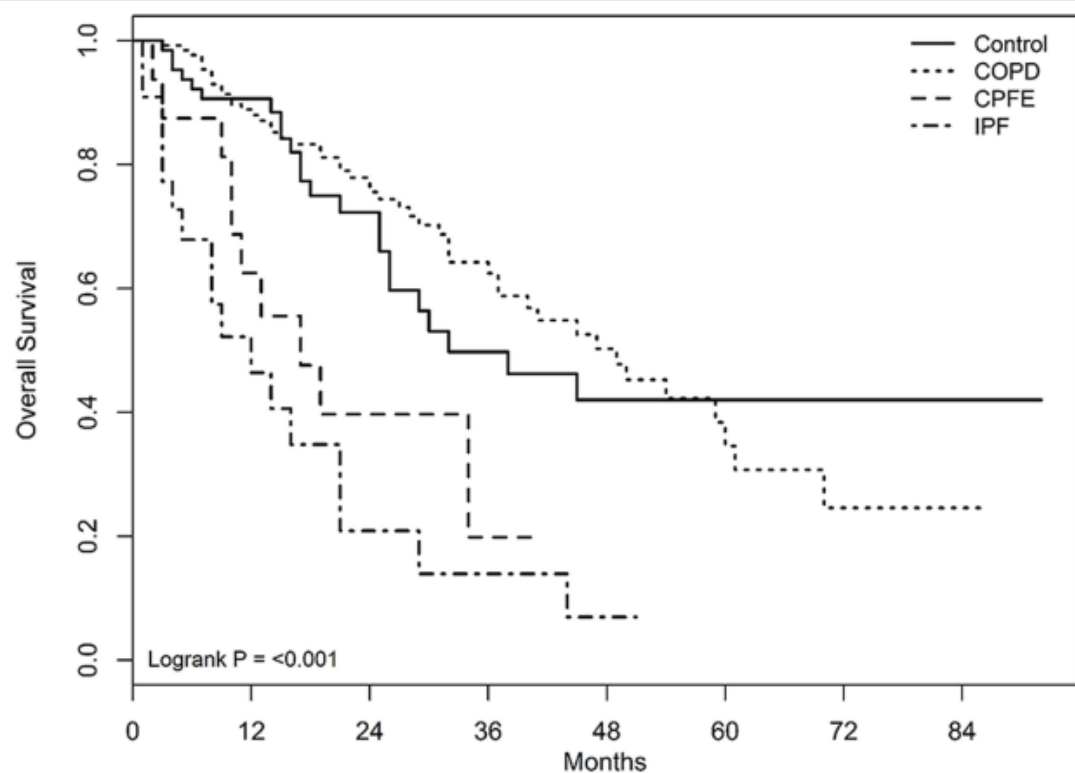
Categories	No. of patients (%)	Median (range)
30-d mortality	46 (2.6)	
30-d mortality by cause of death		
AE	33 (71.7)	
Infection	3 (6.5)	
Pulmonary embolism	1 (2.1)	
Others	9 (19.5)	
AE		
—	1599 (90.7)	
+	164 (9.3)*	
Days from operation to AE		7 (0-29)
Outcome of AE		
Alive	92 (56.1)	
Death	72 (43.9)	
Days from AE to death		20 (1-82)
Side of AE		
Operation side	22 (14.2)	
Contralateral	39 (25.2)	
Bilateral	94 (60.6)	

IPF-specific Intraoperative Management

- Use neuraxial/regional anesthesia if indicated
- Low tidal volume strategy if indicated
- Minimize PEEP and FiO₂ if indicated
- Fluid restriction if indicated
- Minimize blood transfusion, if indicated
- Nasogastric decompression if indicated

Risk factors for Radiation pneumonitis

Characteristics	Control*	COPD	CPFE	IPF	P value
All patients (N=234)	64	132	16	22	
≥ Grade 3 RP	1 (1.6%)	3 (2.3%)	1 (6.3%)	7 (31.8%)	<0.001
Subgroup analysis with stage I NSCLC (N=170)	48	96	11	15	
≥ Grade 3 RP	0 (0.0%)	2 (2.1%)	1 (9.1%)	4 (26.7%)	<0.001
Subgroup analysis with stage II NSCLC (N=64)	16	36	5	7	
≥ Grade 3 RP	1 (6.3%)	1 (2.8%)	0 (0.0%)	3 (42.9%)	0.003



Risk factors for SBRT pneumonitis



RTOG	CTCAE v. 5.0	SWOG
Grade 0 No changes	No changes	Normal
Grade 1 Asymptomatic or mild symptoms	Asymptomatic, only radiological, or tomographic findings	Radiographic changes, symptoms do not require steroids
Grade 2 Moderate symptoms of pneumonitis (severe cough) and radiographic changes (radiographic patches)	Symptomatic, does not interfere with daily activities	Steroids required or tap of effusion
Grade 3 Severe symptoms of pneumonitis, dense radiographic changes	Symptomatic, interferes with daily activities, requires supplemental O2	Oxygen required
Grade 4 Symptoms of severe respiratory failure requiring assisted ventilation or continuous O2	Threatens life, requires mechanical ventilation support	Requires assisted ventilation
Grade 5 Death-related late effects of radiotherapy	Death related severe pneumonitis	–

Study	Number of patients	Number of patients with ILD	Rate of 2+ RP			Rate of Grade 3+ RP		
			ILD	Non-ILD	P-value	ILD	Non-ILD	P-value
Tsurugai et al ⁷³	508	42	19%	15%	.46	12%	3%	.009
Glick et al ⁷¹	537	39	20.5%	5.8%	<.01	10.3%	1.0%	<.01
Bahig et al ⁷⁰	504	28	NA	NA	NA	32%	2%	<.001
Ueki et al ⁷⁴	157	20	55%	13%	<.0001	10%	1.5%	.02
Yoshitake et al ⁷⁵	260	18*	50%	6.7%	NA	38.9%	2.2%	NA
Yamaguchi et al ⁷²	100	16	19%	10%	NA	19%	3.5%	NA

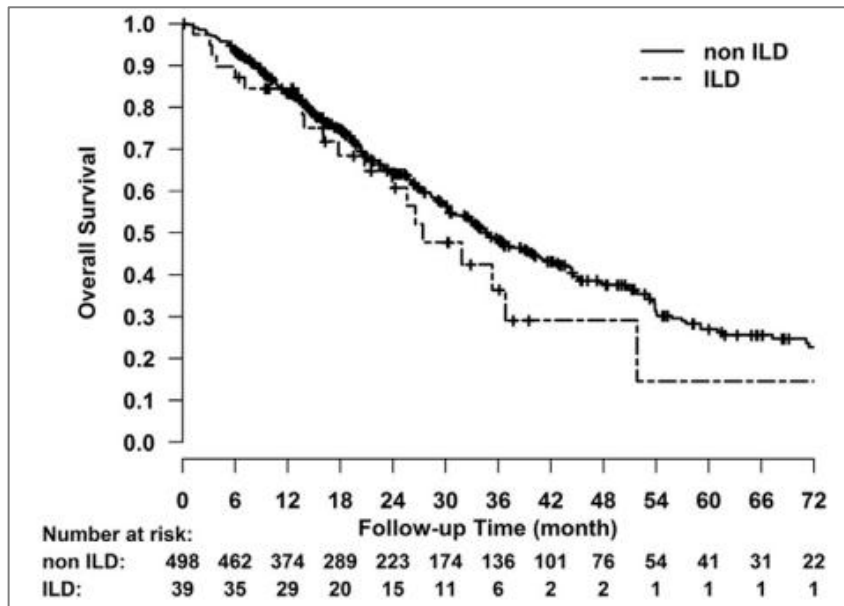
Risk factors for Radiation pneumonitis

- Dosimetric predictors

Factors	Grade ≥ 2 RP			Grade ≥ 3 RP		
	Odds ratio (OR)	95% CI	<i>p</i> value	OR	95% CI	<i>p</i> value
MLD (≥ 12.0 Gy vs. < 12.0 Gy)	2.480	1.006–6.113	0.049	–	–	–
Tumor located in lower lobe	2.311	0.898–5.943	0.082	–	–	–
Chemotherapy with gemcitabine in the past	–	–	–	3.209	1.018–10.113	0.046
V5 ($\geq 50\%$ vs. $< 50\%$)	–	–	–	3.429	1.056–11.140	0.040
Percentage of lung volume affected in subclinical ILD $\geq 25\%$	–	–	–	4.861	1.237–19.104	0.024

RP, radiation pneumonitis; MLD, mean lung dose; V5, percentage of lung volume receiving ≥ 5 Gy; ILD, interstitial lung disease; CI, confidence interval

- OS



Proposal for Therapeutic Strategies



TABLE 1 Suggestions for treatment of lung cancer in fibrosing interstitial lung disease (fILD)

Suggestions based on the available studies:

The choice of treatment with chemotherapy should be carefully made by analysis of the risk/benefit balance. Patient selection and careful counselling are crucial.

Carboplatin plus weekly (nab-)paclitaxel for four (or six) cycles remains the first-line standard therapy in fit NSCLC fILD patients without maintenance therapy.

Addition of bevacizumab should be considered in fit nonsquamous NSCLC patients.

Vinorelbine (squamous) and pemetrexed (adenocarcinoma) monotherapy should be administered in a second-line setting.

Carboplatin etoposide for four cycles (or six cycles) remain the standards of care for SCLC.

Drugs that are not recommended: gemcitabine and docetaxel.

NSCLC: nonsmall cell lung cancer; SCLC: small cell lung carcinoma.

Risk factors for CTx-pneumonitis

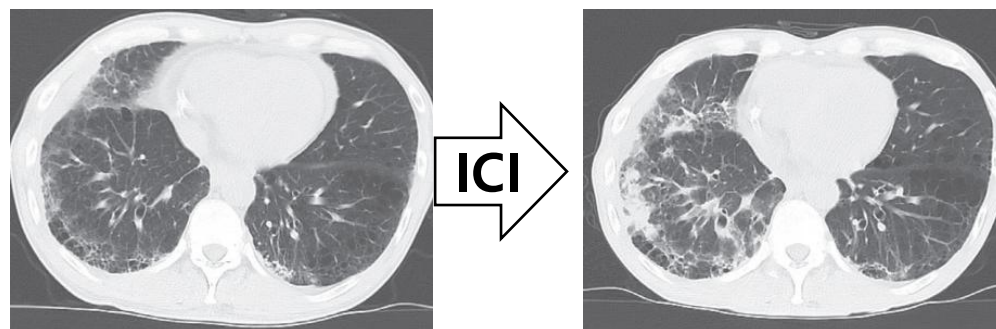
Regimen	n	ORR (%)	DCR (%)	AE (n)	AE incidence (%)
< NSCLC >					
Tri-weekly CBDCA + PTX	113	32.7	62.8	13	11.5
CBDCA + PEM	61	21.3	54.1	10	16.4
CBDCA + S-1	42	23.8	50.0	2	4.8
CBDCA + PTX + Bev	32	59.4	81.3	4	12.5
CDDP + PEM	26	38.5	57.7	3	11.5
DTX	26	11.5	34.6	9	34.6
CBDCA + nab-PTX	26	42.3	69.2	1	3.8
CBDCA + PEM + Bev	23	43.5	87.0	3	13.0
Weekly CBDCA + PTX	21	42.9	71.4	1	4.8
PEM	17	11.8	23.5	3	17.6
CDDP + DTX	15	60.0	80.0	2	13.3
S-1	13	0	38.5	2	15.4
VNR	12	8.3	33.3	3	25.0
CDDP + VNR	11	27.3	63.6	0	0
CBDCA + VP16	11	9.1	45.5	1	9.1
Others [†]	43	–	–	5	11.6
Total	492	29.3	58.7	62	12.6
< SCLC >					
CBDCA + VP16	160	51.2	64.4	5	3.1
CDDP + VP16	34	52.9	70.6	2	5.9
CDDP + CPT11	10	50.0	80.0	0	0
CBDCA + CPT11	6	66.7	66.7	1	16.7
Others ^{**}	6	–	–	1	16.7
Total	216	51.4	65.7	9	4.2

Risk factors for ICI-pneumonitis

Table 2: Outcomes of patients with interstitial lung disease receiving immune checkpoint inhibitors

Study	ILD study population	Key findings
Tasaka et al ⁵⁵	416 patients with advanced or recurrent NSCLC, 49 of whom had ILD, treated with nivolumab or pembrolizumab 30.6% vs 9.5%	Increased incidence of pneumonitis in the group with pre-existing ILD compared to the non-ILD group (30.6% compared with 9.5%). Non-inferior progression-free and overall survival in the pre-existing ILD group compared to controls.
Nakanishi et al ⁵⁶	83 patients with NSCLC, 13 of whom had ILA, treated with nivolumab or pembrolizumab 42.9% vs 10.1%	Incidence of ICI-ILD* was higher in the group of subjects with pre-existing ILA compared with those without ILA (42.9% vs. 10.1%, $P = .007$). In the ILA group, ground-glass attenuation was associated with increased risk of ICI-ILD.
Shimoji et al ⁶³	199 subjects with non-lung cancers, 37 (18.6%) of whom had ILA, treated with nivolumab or pembrolizumab	Presence of ILA was associated with increased risk of developing ICI-ILD. For those with ILA, the presence of ground-glass attenuation was associated with the development of ICI-ILD.
Kanai et al ⁵⁷	216 patients with NSCLC, including 26 with ILD, treated with nivolumab. 31% vs 12%	Higher incidence (31% vs 12%) and severity (19% vs. 5%) of pneumonitis in the ILD group compared with the non-ILD group. No pneumonitis-associated deaths.
Fujimoto et al ⁵⁸	18 patients with NSCLC and mild IIP defined as vital capacity greater than 80% predicted and a possible UIP or inconsistent with UIP pattern treated with nivolumab.	Two cases of grade 2 pneumonitis. No deaths related to nivolumab treatment.
Nishiyama et al ⁵⁹	48 patients with advanced NSCLC with ILD treated with nivolumab, pembrolizumab, or atezolizumab	7 subjects (14.5%) developed AE-ILD. The occurrence of AE-ILD was associated with ground-glass attenuation score prior to ICI administration.
Shibaki et al ⁶⁰	331 patients with NSCLC, including 17 with ILD, treated with nivolumab or pembrolizumab 29% vs 10%	Pneumonitis incidence was higher in subjects with underlying ILD compared with those without (29% vs. 10%, $P = .027$).
Yamaguchi et al ⁶¹	123 subjects with NSCLC, including 37 with a fibrosis score ≥ 1 , treated with nivolumab or pembrolizumab	18 patients developed ICI-related pneumonitis (14.6%) with fibrosis score on CT of ≥ 1 being a risk factor for ICI-related pneumonitis
Dobre et al ⁶²	41 patients with ILD and cancer (73.2% with lung cancer) treated with nivolumab or pembrolizumab	3 subjects (7.3%) developed ICI-related pneumonitis. At 1 year, most deaths were cancer related (69.6%) or due to non-cancer and non-ILD etiologies (17.4%) compared with 13% of deaths related to ILD or ICI pneumonitis.

Risk factors for ICI-pneumonitis

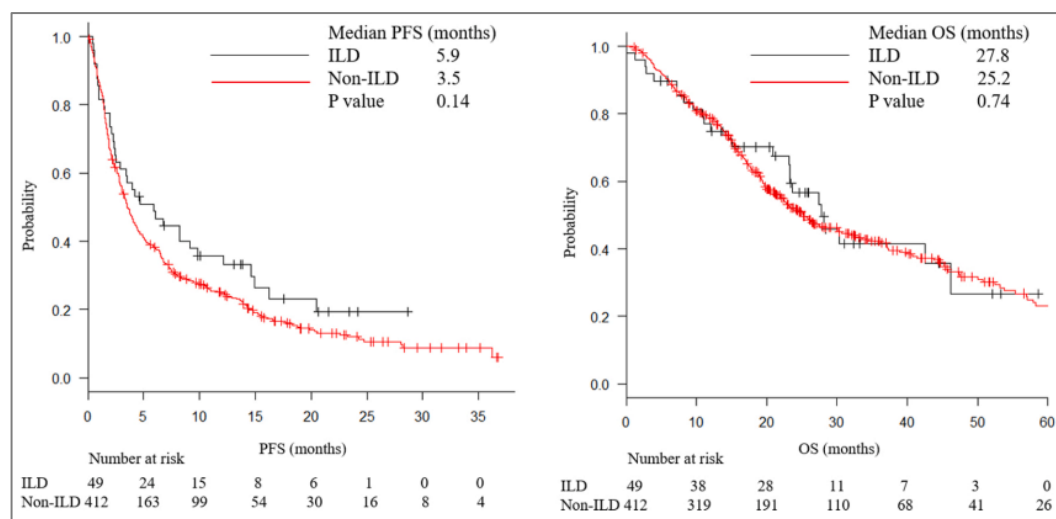


Thorac Cancer 2018 9(7):847-855

Factors		Total	ILD group All patterns	UIP pattern	NSIP pattern	Non-ILD group	P
n		216	26	12	14	190	
ILD		30 (14)	8 (31)	3 (25)	5 (36)	22 (12)	0.014
ILD grade	1, 2	15 (50)	3 (38)	0 (0)	3 (60)	12 (55)	0.022
	3, 4	15 (50)	5 (62)	3 (25)	2 (14)	10 (45)	
Time to onset (months)		2.3 (0.07–13.1)	2.3 (0.7–4.4)	0.9 (0.7–2.3)	2.7 (1.1–4.4)	2.3 (0.07–13.1)	0.433

19%

5%



- ILD should not be considered as absolute C/lx for IO

Lung Cancer 2021 155:120-126

Anti-fibrotics and Postoperative AE



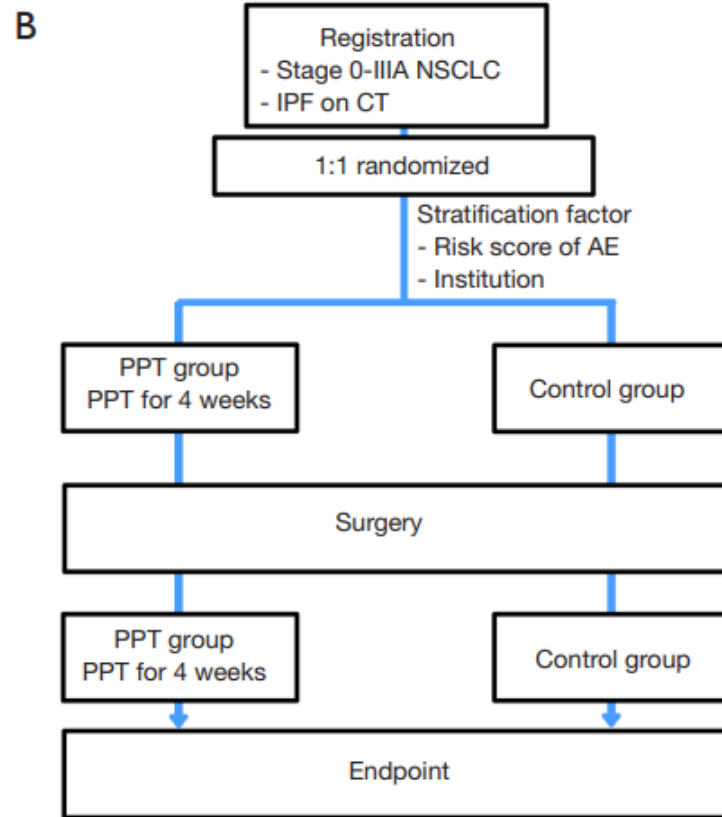
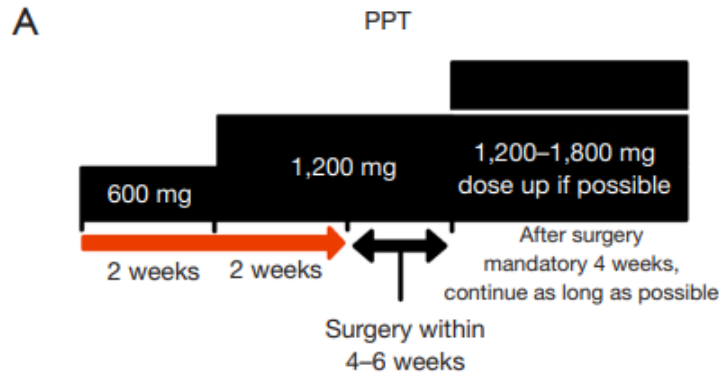
TABLE 2 Core features of studies of post-operative outcomes, comparing patients treated and not treated with peri-operative pirfenidone (poPirf)

First author [ref.]	Cohort size, treated and untreated arms	Study design	Post-operative AE-IPF	Post-operative mortality
IWATA [101]	n=50 poPirf n=33 No poPirf n=17	Retrospective poPirf for 4 weeks before and after surgery	Reduction in AE-IPF with poPirf at 30 days (0% versus 10.5%, p=0.07) and at 90 days (3.2% versus 21.1%, p=0.04) 3.2% vs 21.1%	IPF progression-free survival curves difference between groups was statistically marginal (p=0.0676), better in the poPirf group poPirf was numerically, but not significantly, associated with better IPF progression-free survival
SEKIYARA [102]	n=56 poPirf n=36 No poPirf n=20	Retrospective poPirf for 4 weeks before surgery; "longer periods" after surgery	Reduction in AE-IPF with poPirf (8%) compared with no poPirf (20%) Nonsignificant trend (p=0.21) 8% vs 20%	Reduced mortality in poPirf group (p=0.04)

Table 1. Impact of antifibrotics on survival of patients with idiopathic pulmonary fibrosis and lung cancer

Study	Study design	Patients	Outcome measure	Results
Karampitsakos et al. (2023) [11]	Multicenter, retrospective	98 (antifibrotics) vs. 98 (no antifibrotics)	All-cause mortality	Unadjusted hazard ratio, 0.61 (95% CI, 0.42–0.87)
Naai et al. (2022) [36]	Multicenter, retrospective	5 lung cancer out of 189 IPF patients with antifibrotics vs. 30 lung cancer out of 156 patients (no antifibrotics)	Lung cancer-related mortality	Risk ratio, 0.106 (95% CI, 0.025–0.450)
Samsung Medical Center (unpublished)	Single-center, retrospective	79 (antifibrotics) vs. 512 (no antifibrotics)	5-year survival rate	20.3% (antifibrotics) vs. 46.1% (no antifibrotics) (P<0.001)

Pirfenidone and Postoperative AE (NEJ034)



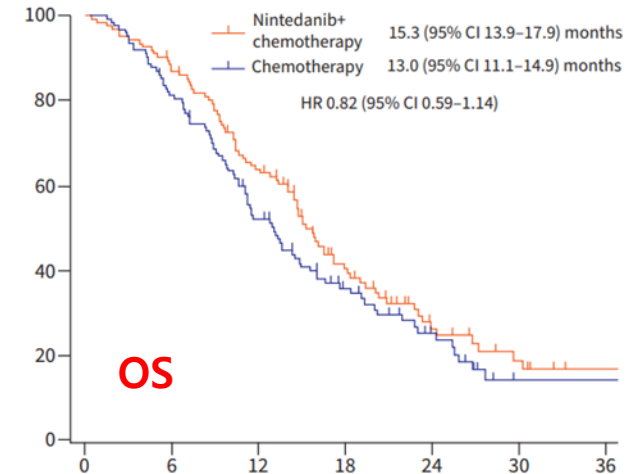
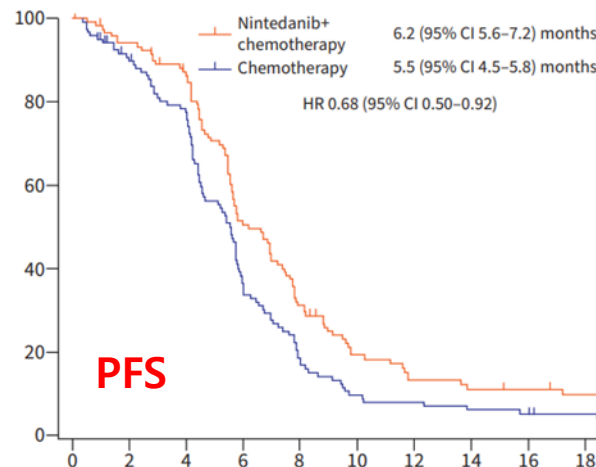
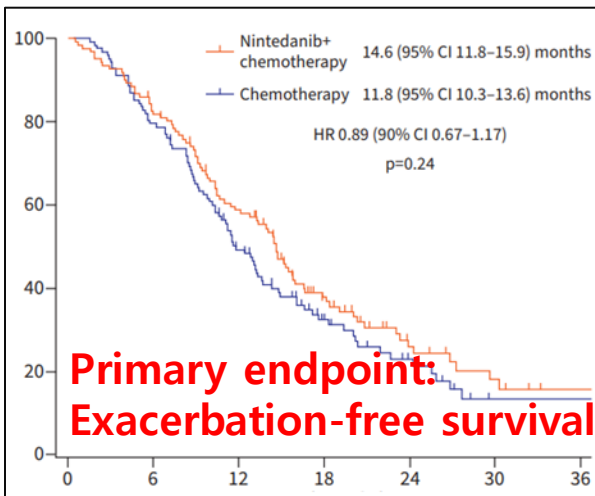
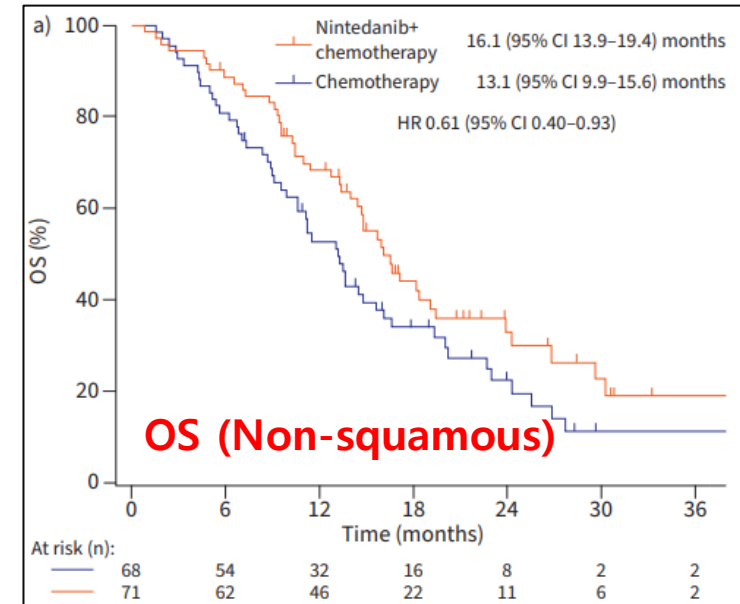
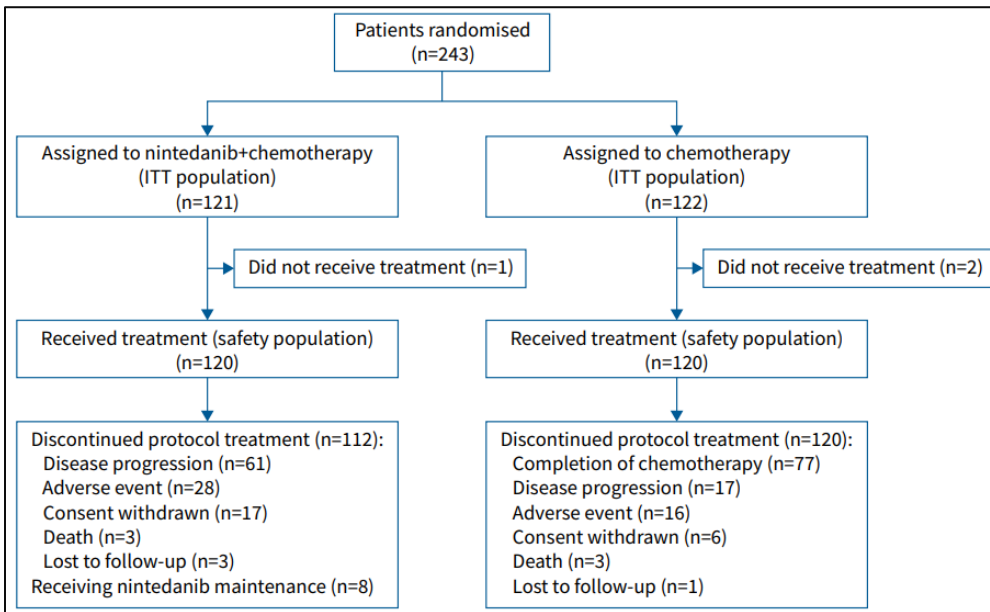
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Phase III trial of perioperative pirfenidone therapy for lung cancer with idiopathic pulmonary fibrosis (IPF): NEJ034 study

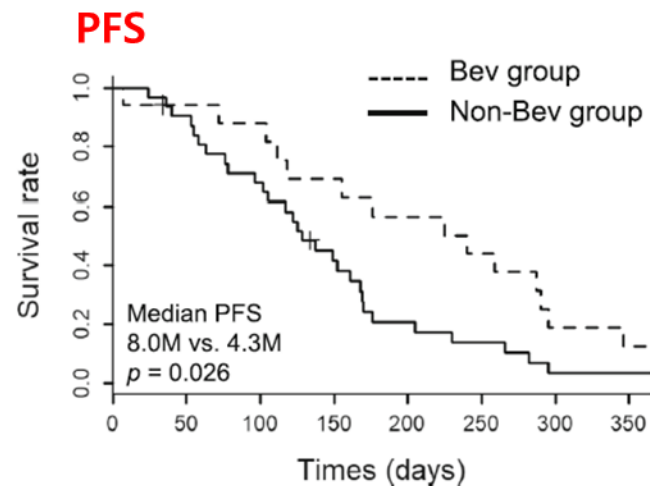
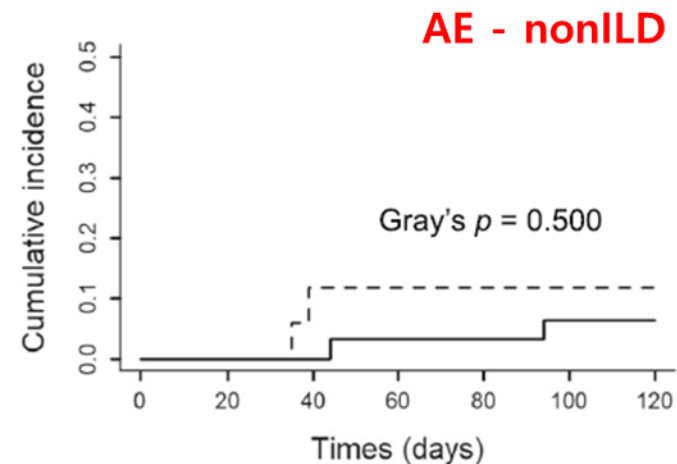
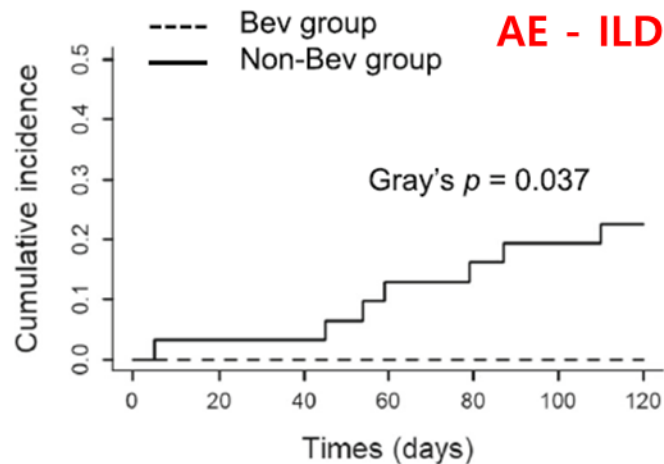
Results: Two hundred thirty-two patients were enrolled, and 116 were allocated to the trial treatment and control, respectively. AE within 30 days postoperatively occurred in 20 patients (8.7%). One patient was excluded by central review, and seven patients (6.1%) experienced events in the trial treatment cohort; on the contrary, 12 patients (10.3%) in the control cohort did not have a significant difference ($p=0.339$) in the full analysis set.

Conclusions: The planned number of patients enrolled in this study was completed within the study period, although the primary endpoint was not met. Then, in addition to the secondary analysis, the efficacy of other endpoints or safety information in the per protocol set will be investigated based on the central review.

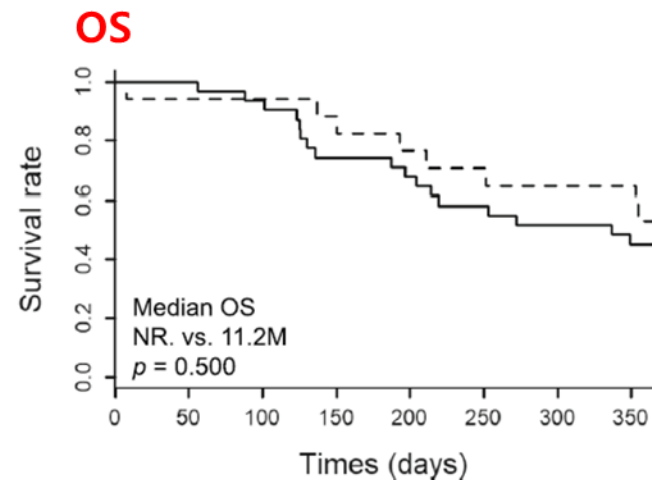
Anti-fibrotics for CTx-pneumonitis



Bevacizumab for CTx-pneumonitis



No. at risk								
Bev group	17	15	15	12	10	8	4	3
Non-Bev group	31	29	22	13	7	5	2	2

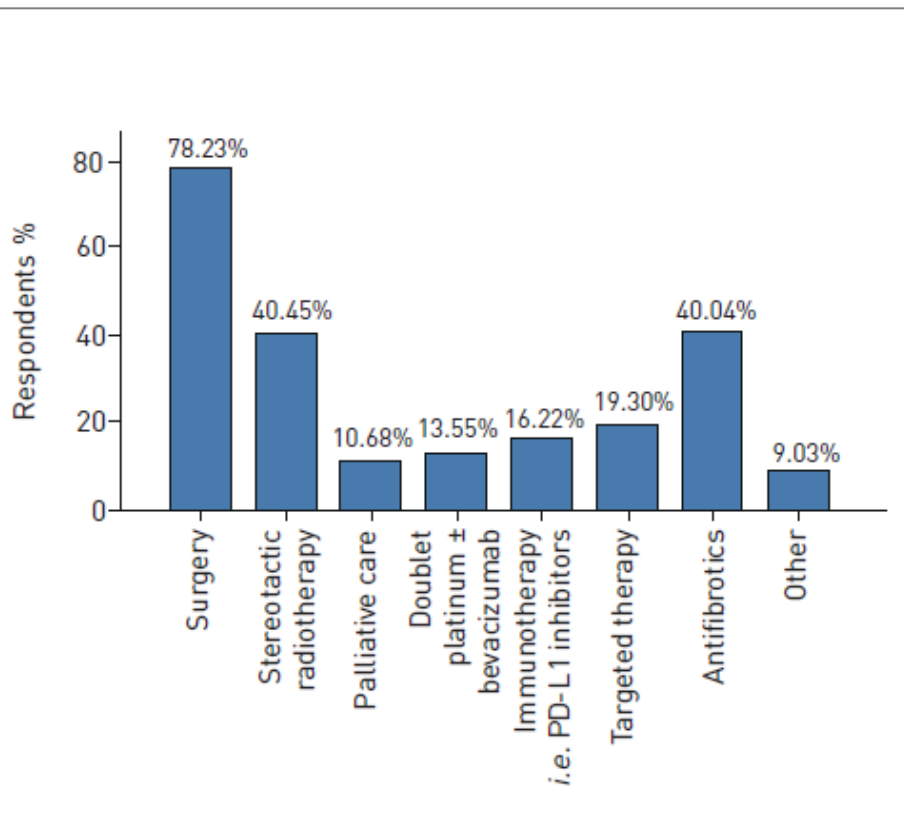


No. at risk								
Bev group	17	16	16	16	14	13	12	12
Non-Bev group	31	31	30	24	22	19	17	15

International Survey

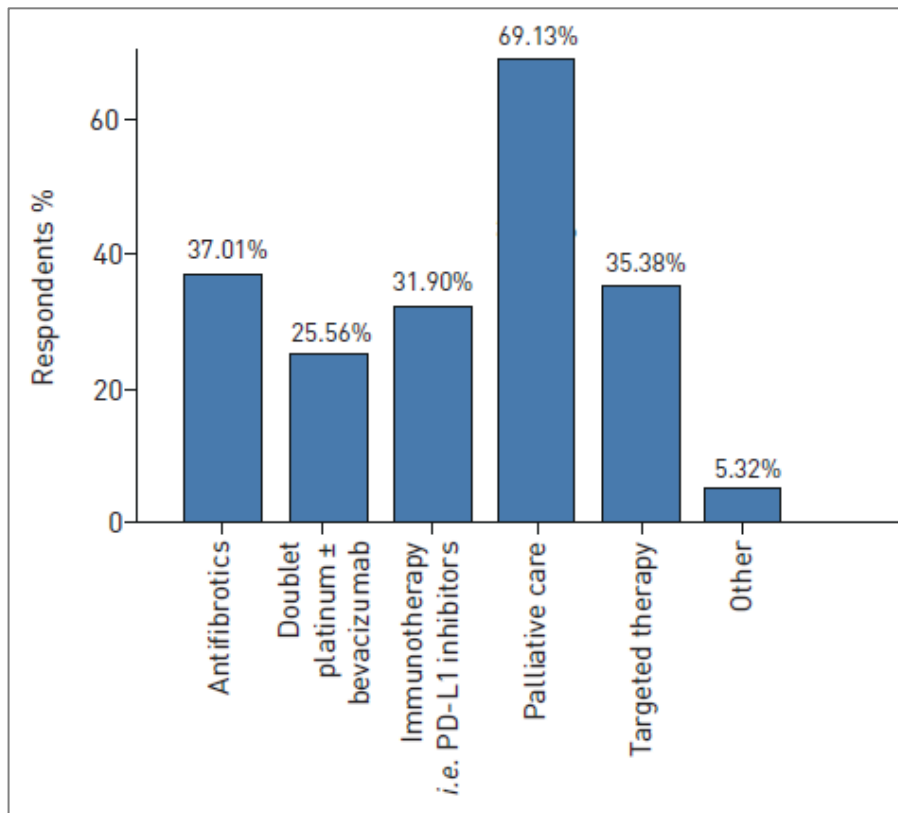
Mild-to-Moderate IPF (DLco>35%, FVC>50%)

Stage I NSCLC



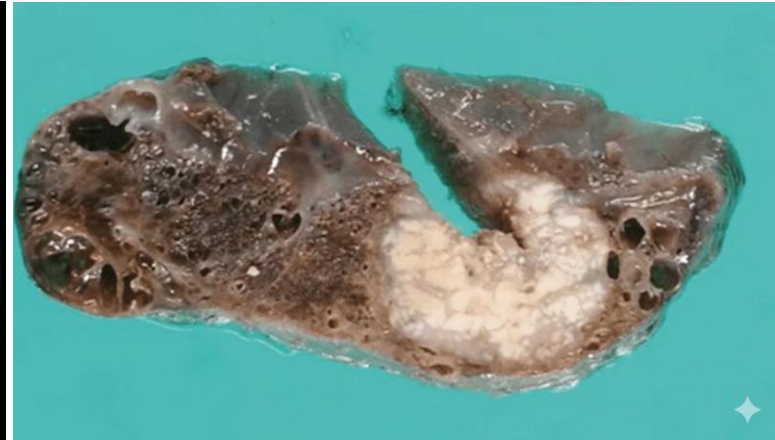
Advanced IPF (DLco<35%, FVC<50%)

Stage IV NSCLC

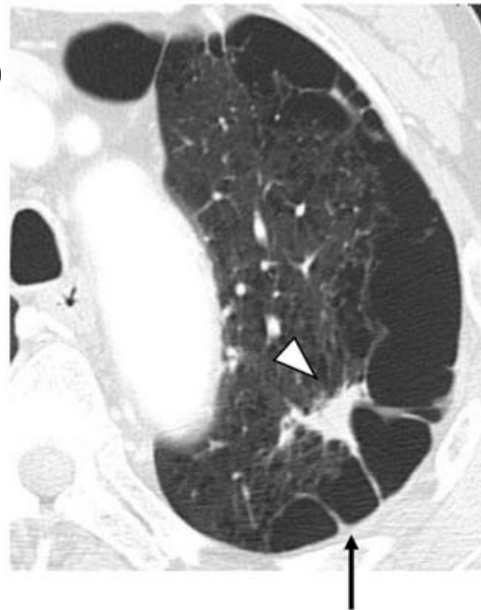


Today's Contents

- IPF



- COPD (emphysema)



Common Pathogenic Mechanism

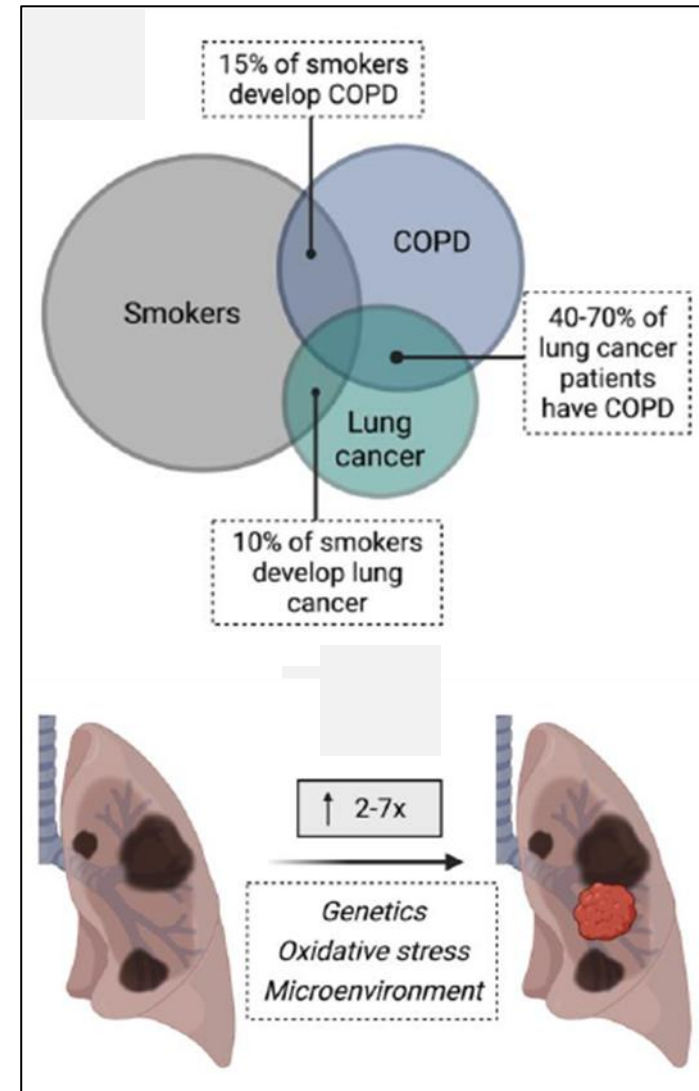
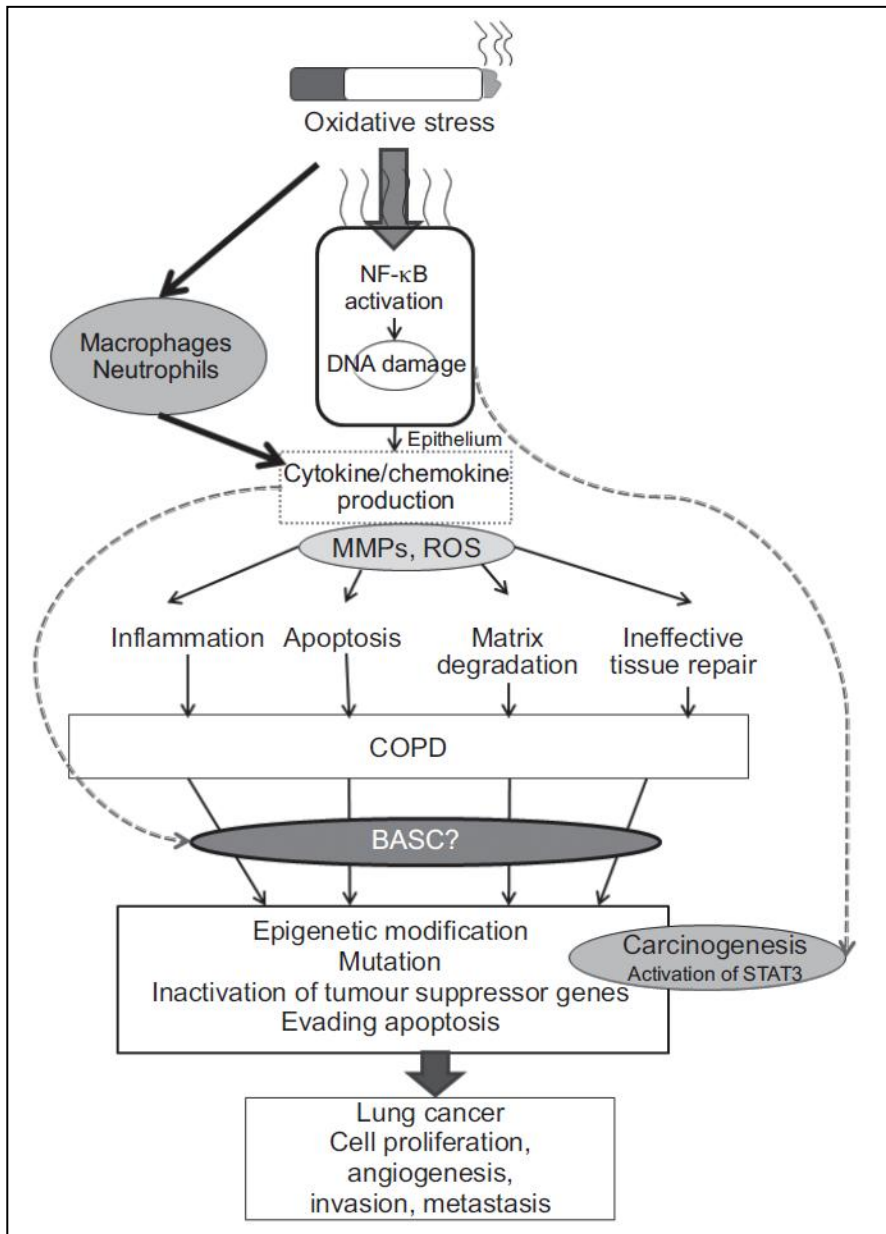


Table 1 Major causes of death reported in patients with chronic obstructive pulmonary disease

Author	Publication year	Total No. of COPD	Total deaths	Cause of death (%) ¹			
				COPD ²	Lung cancer	Other cancer	Cardiovascular
Vilkman <i>et al</i> ^[14]	1997	2237	1070	30	12	8	33
Garecka <i>et al</i> ^[11]	1997	135	70	61	4	4	6
Antonelli Incalzi <i>et al</i> ^[6]	1997	270	228	63	5	4	16
Zielinski <i>et al</i> ^[15]	1997	215	215	49	7	ND	37
Keistinen <i>et al</i> ^[12]	1998	2727	973	22	13	8	32
Pauwel <i>et al</i> ^[13]	1999	1277	18	6	33	6	39
Garcia-Aymerich <i>et al</i> ^[10]	2003	340	98	74	5	2	12
Celli <i>et al</i> ^[9]	2004	625	162	61	12	ND	14
Anthonisen <i>et al</i> ^[16]	2005	5887	731	8	33	21	22

Table 2 Odds ratios for coincidental lung cancer based on factors indicative of chronic obstructive pulmonary disease or interstitial lung diseases, according to smoking status¹

	Never smoker (<i>n</i> = 284)	Ex-smoker (<i>n</i> = 101)	Current smoker (<i>n</i> = 179)	Total (<i>n</i> = 564)
FEV1/FVC < 70%	10.42 (2.82-38.55) ³	5.89 (2.02-17.22)	7.456 (3.48-15.95)	7.17 (4.03-12.74)
%VC < 80%	2.02 (0.42-9.86)	No data ⁴	2.25 (0.62-8.11)	4.73 (2.00-11.17)
LAA score ≥ 1 ²	0.98 (0.21-4.43)	3.43 (1.50-7.85)	5.07 (2.51-10.28)	3.63 (2.24-5.89)
Fibrosis score ≥ 1	6.39 (2.13-19.18)	3.94 (1.20-12.88)	5.45 (2.39-12.44)	5.10 (2.82-9.24)
GGA score ≥ 1	2.32 (0.80-6.71)	3.59 (1.09-11.80)	2.48 (1.06-5.77)	2.71 (1.52-4.81)

Epidemiology

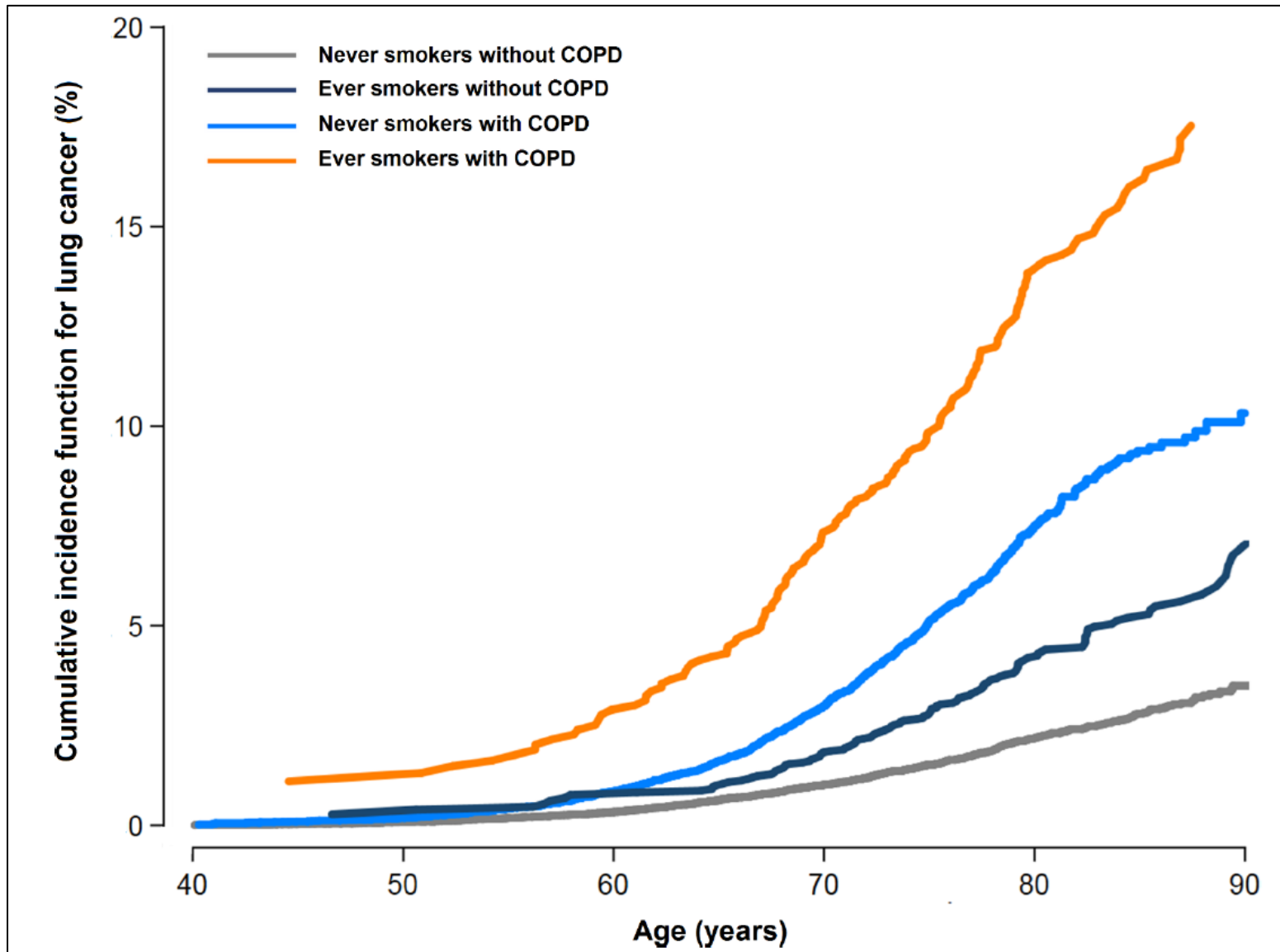
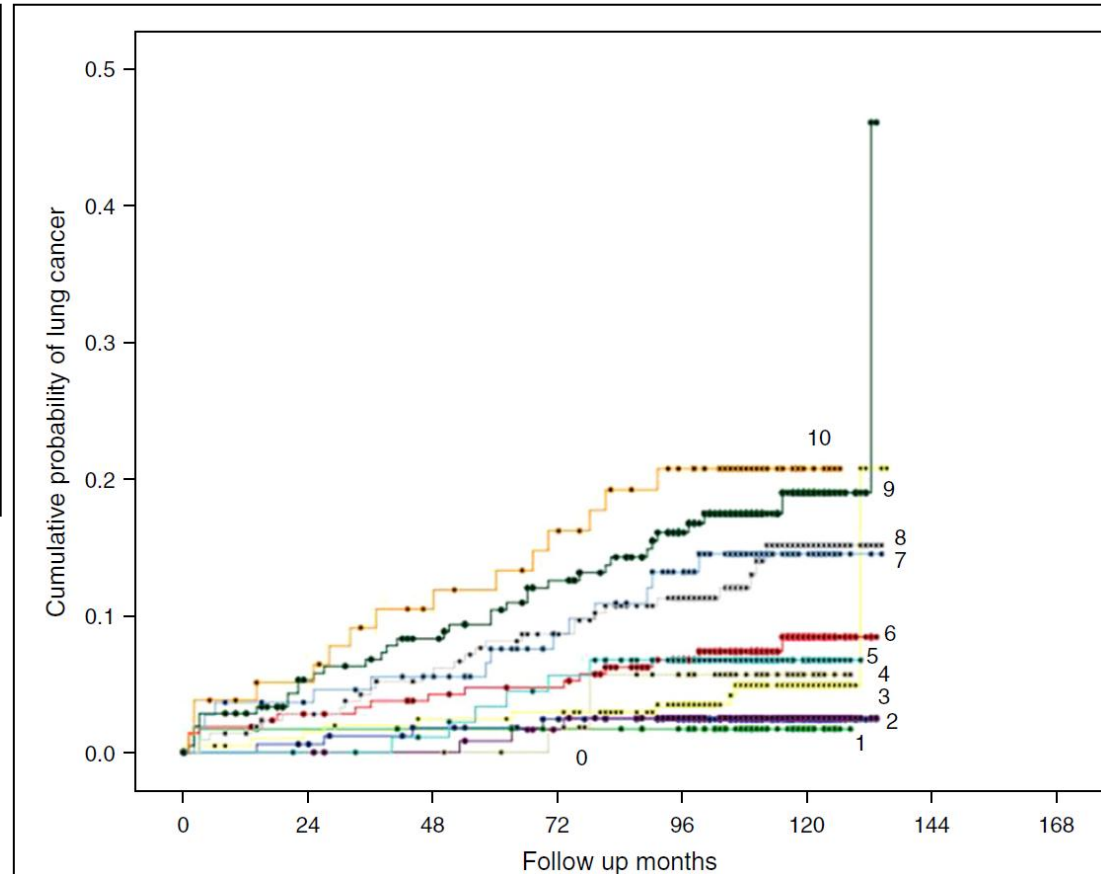


Table 1. COPD-LUCSS

	Score (Points)
BMI <25	1
Pack-years history >60	2
Age >60 yr	3
Radiologic emphysema, yes	4
Total	10



Features of COPD as Predictors of Lung Cancer

Factor	Lung Cancer Diagnosis			
	Model 1		Model 2	
	OR (95% CI)	P Value	OR (95% CI)	P Value
FEV ₁ /FVC per 10% decrease	1.28 (1.12-1.46)	< .001	–	
FEV ₁ ppd per 5% decrease	...		1.07 (1.03-1.12)	< .001
Exacerbations in year prior to enrollment per event increase (0, 1, and ≥ 2)	1.39 (1.04-1.85)	.02	1.37 (1.02-1.82)	.03
Visual emphysema: none-trace vs mild-advanced	2.31 (1.41-3.76)	< .001	2.64 (1.66-4.30)	< .001

Chest 2018;153(6):1326-1335

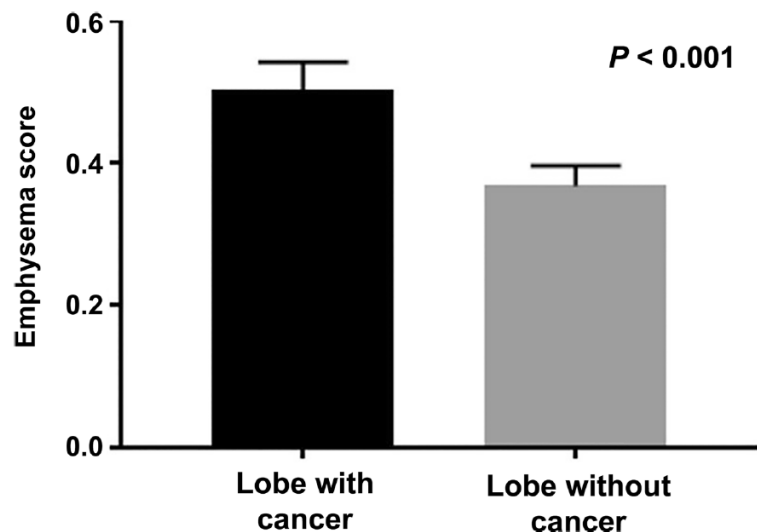
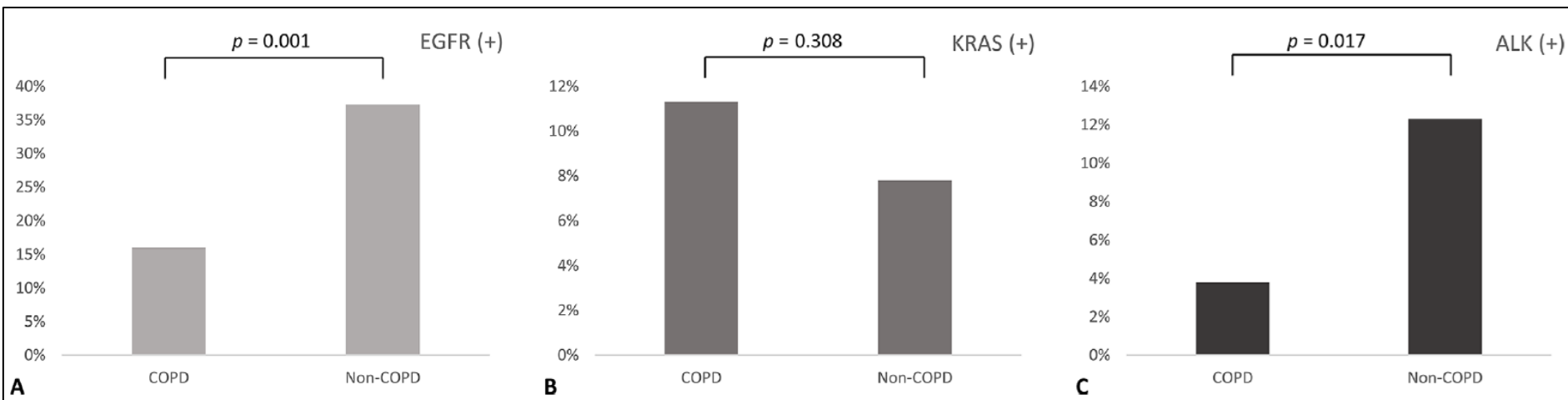


Fig. 1 Difference of regional emphysema score between lobe with cancer and those without cancer in lung cancer patients after lobectomy ($P < 0.001$)

Clinico-pathological characteristics

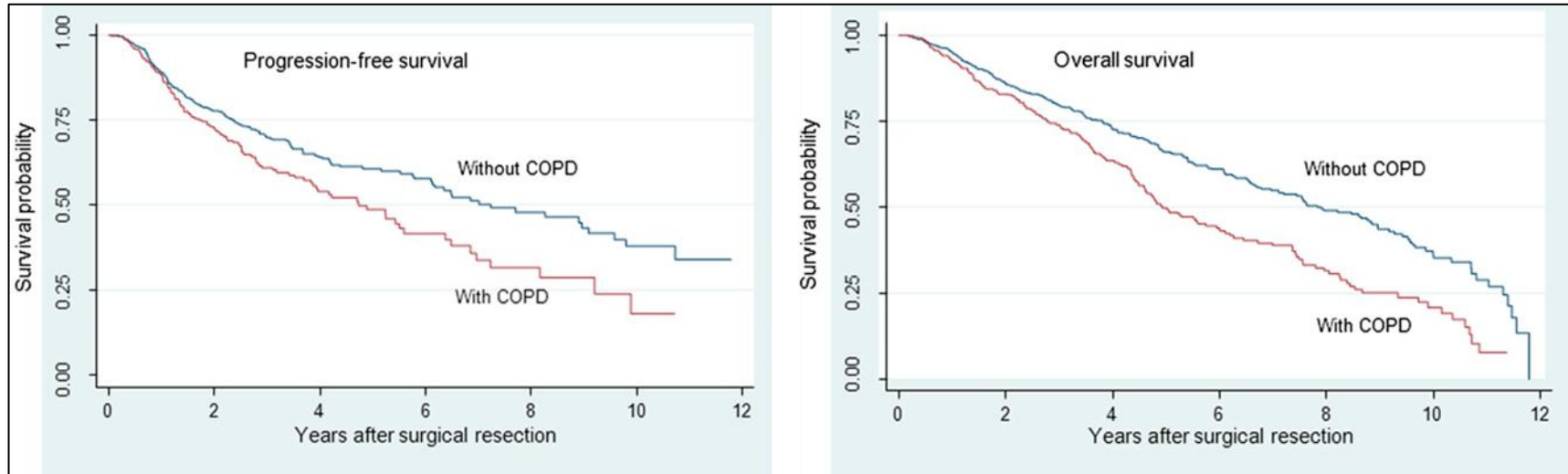


	EGFR			ALK		
	Odds Ratio	95% CI	p-value	Odds Ratio	95% CI	p-value
COPD	0.197	0.065–0.600	0.004	0.487	0.254–0.931	0.029
Age	0.992	0.959–1.025	0.616	1.005	0.981–1.030	0.678
Male	4.217	1.478–12.030	0.007	0.453	0.236–0.868	0.017
Smoking	1.188	0.470–3.004	0.716	0.468	0.234–0.937	0.032
Adenocarcinoma	3.113	0.686–14.117	0.141	3.662	1.062–12.624	0.040

Presence of COPD on prognosis

- Lung cancer underwent Surgery with/without COPD

CHEST 2014;145(2):346-353



- Lung cancer underwent Chemotherapy with/without COPD

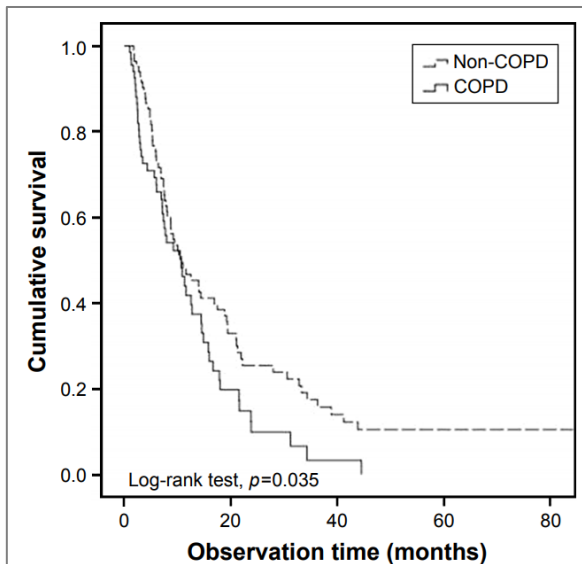


Table 4 Univariate and multivariate analyses of prognostic factors for overall survival in stage IV NSCLC patients (n=151)

Parameter	Univariate analysis			Multivariate analysis		
	Hazard ratio	95% confidence interval	p-value	Hazard ratio	95% confidence interval	p-value
Presence of COPD			0.025			0.039
COPD	1.530	1.054–2.222		1.479	1.020–2.145	
Non-COPD	1			1		

Calculation of predicted postoperative FEV₁ (ppoFEV₁)

Anatomic method (with the knowledge that the lungs contain 19 segments)

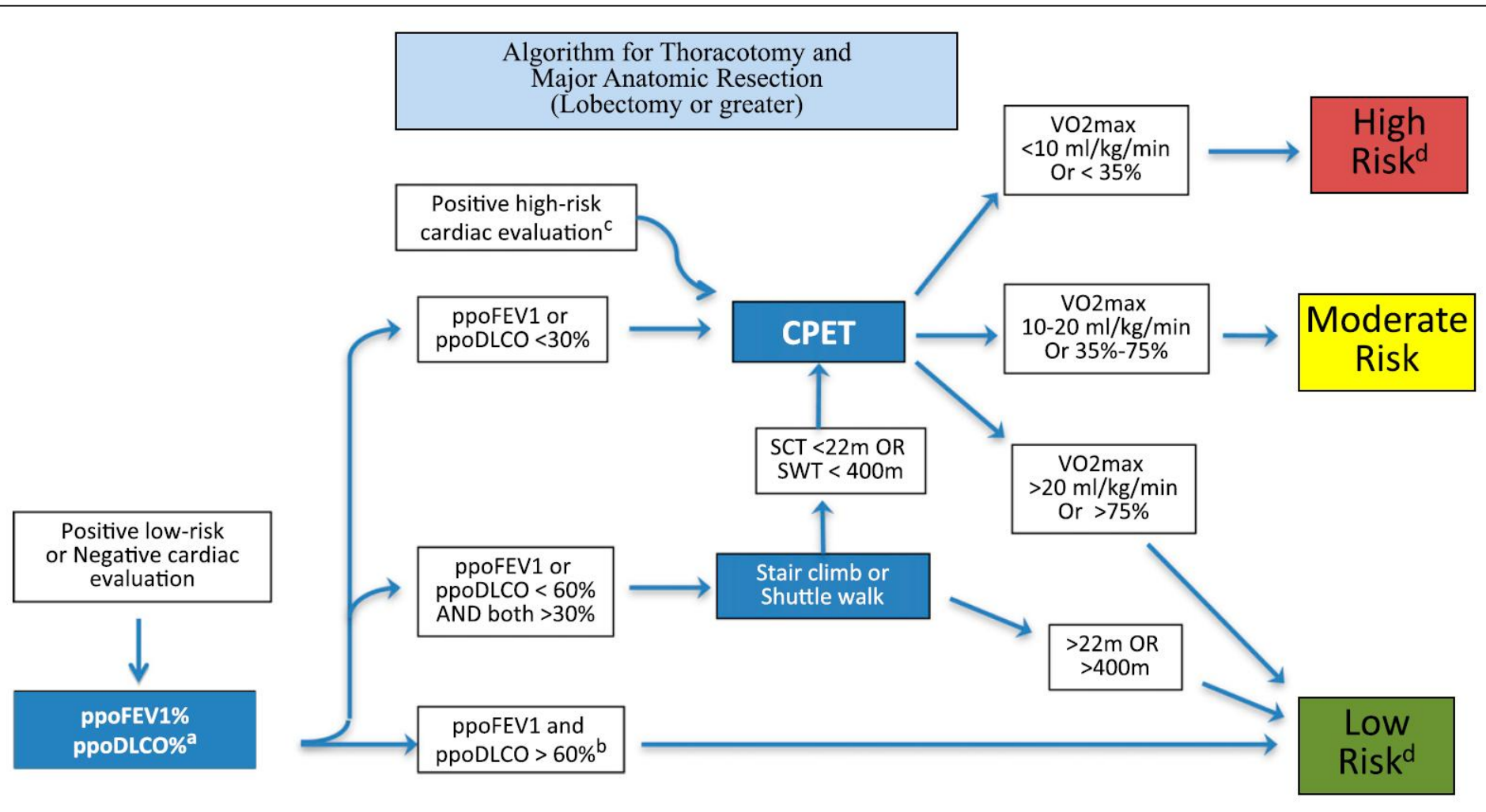
$$\text{ppoFEV}_1 = \text{preoperative FEV}_1 \times \frac{(19 - \text{segments to be removed})}{19}$$

Segments – right: upper lobe, 3; middle lobe, 2; lower lobe, 5
left: upper lobe, 3; lingula, 2; lower lobe, 4

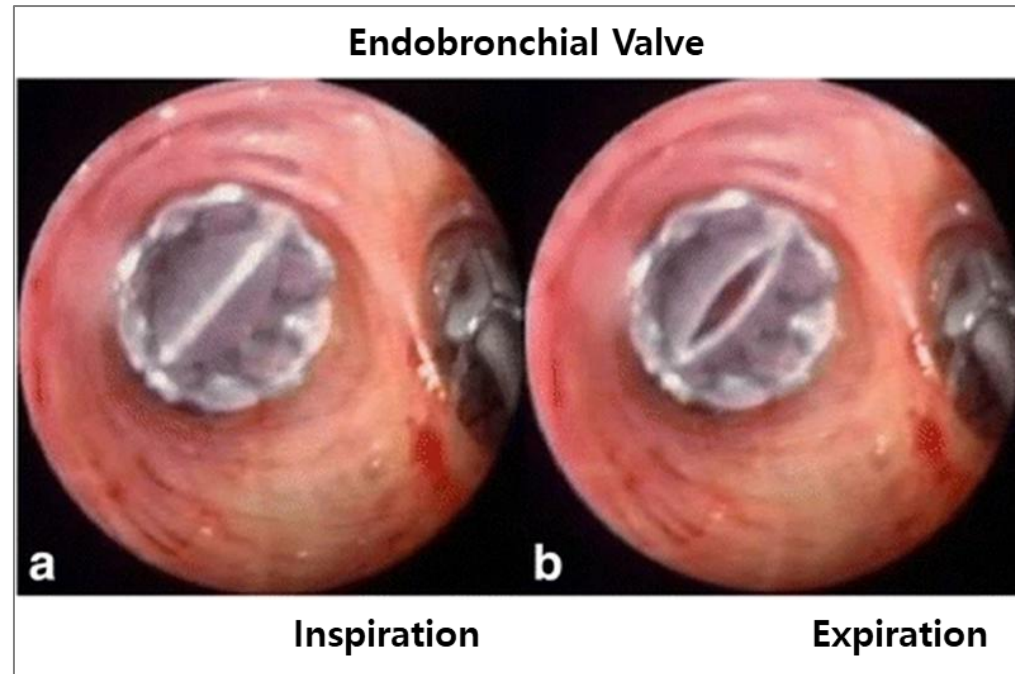
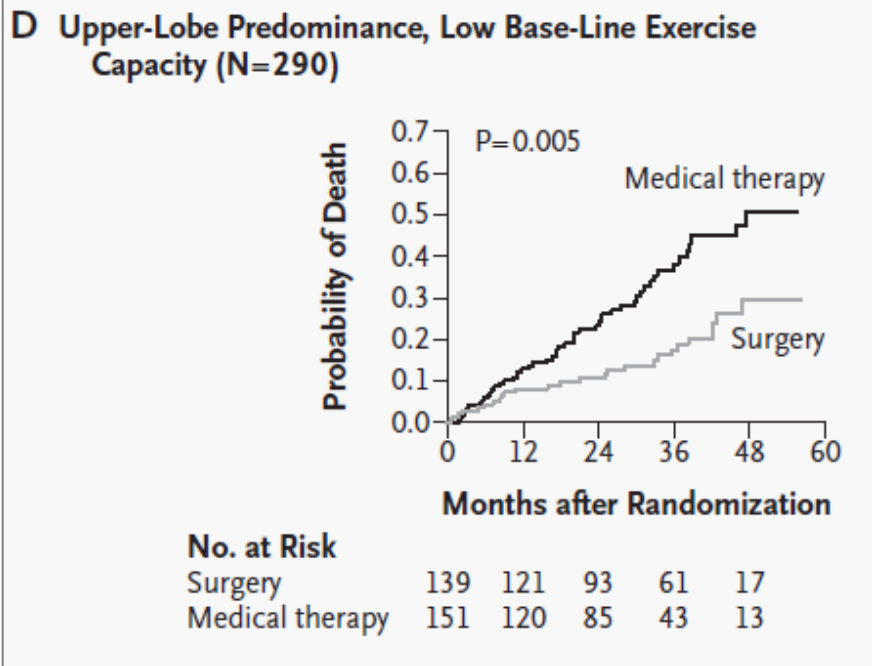
Perfusion method

$$\begin{aligned} \text{ppoFEV}_1 = \\ \text{preoperative FEV}_1 \times (1 - \text{fraction of total perfusion of resected lung}) \end{aligned}$$

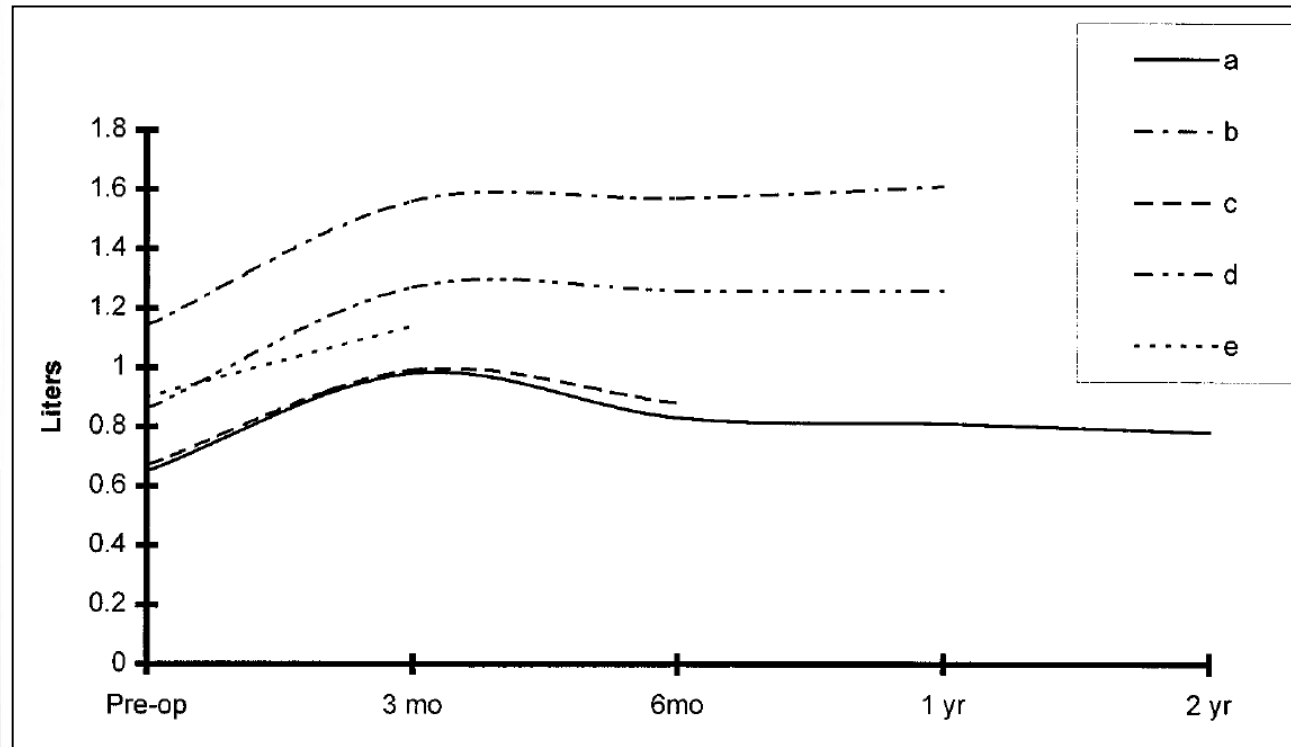
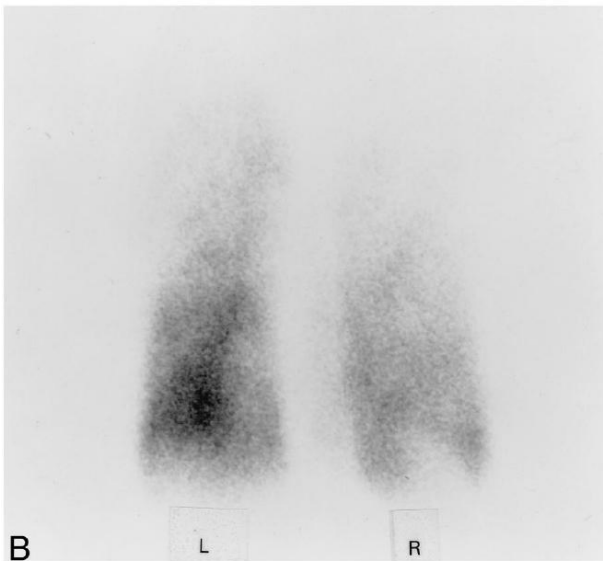
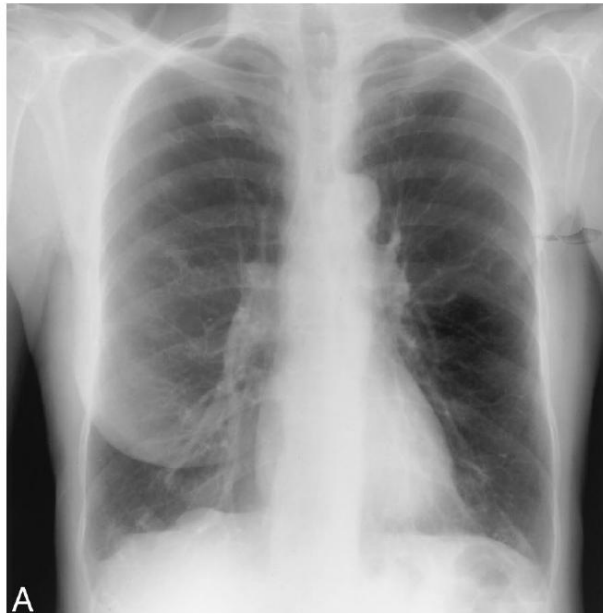
High Risk for Operation



LVRS or Endobronchial Valve



Lobectomy with Volume Reduction



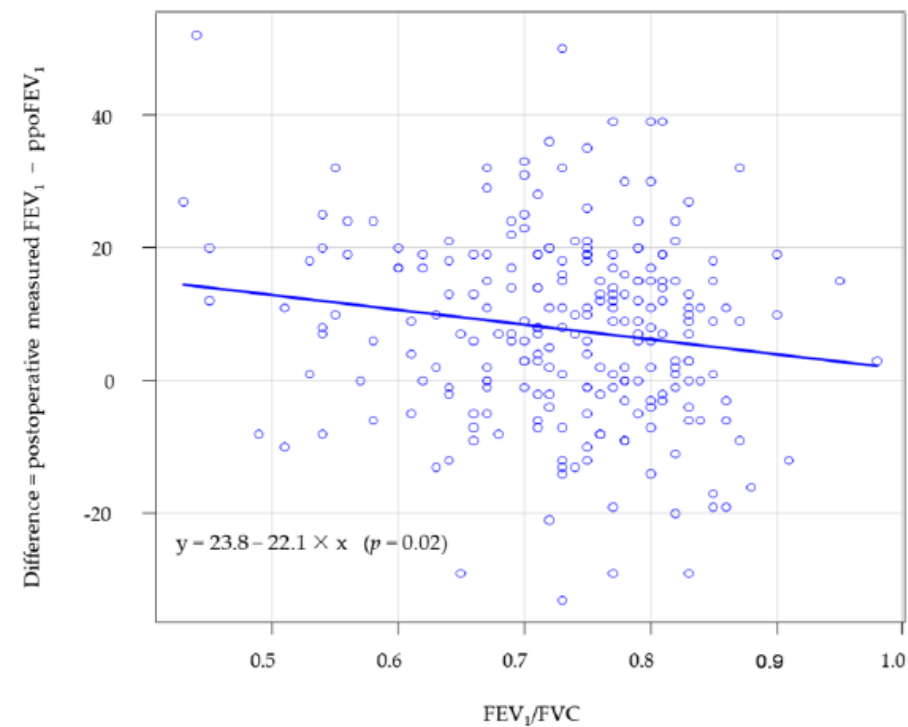
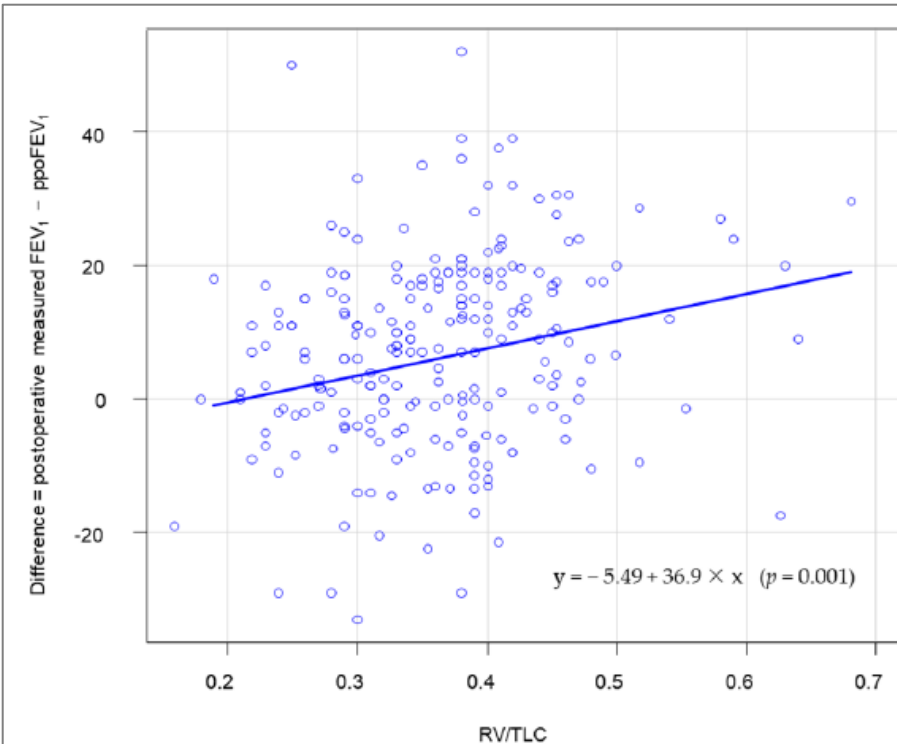
Postoperative Lung Function Changes



Journal of
Clinical Medicine

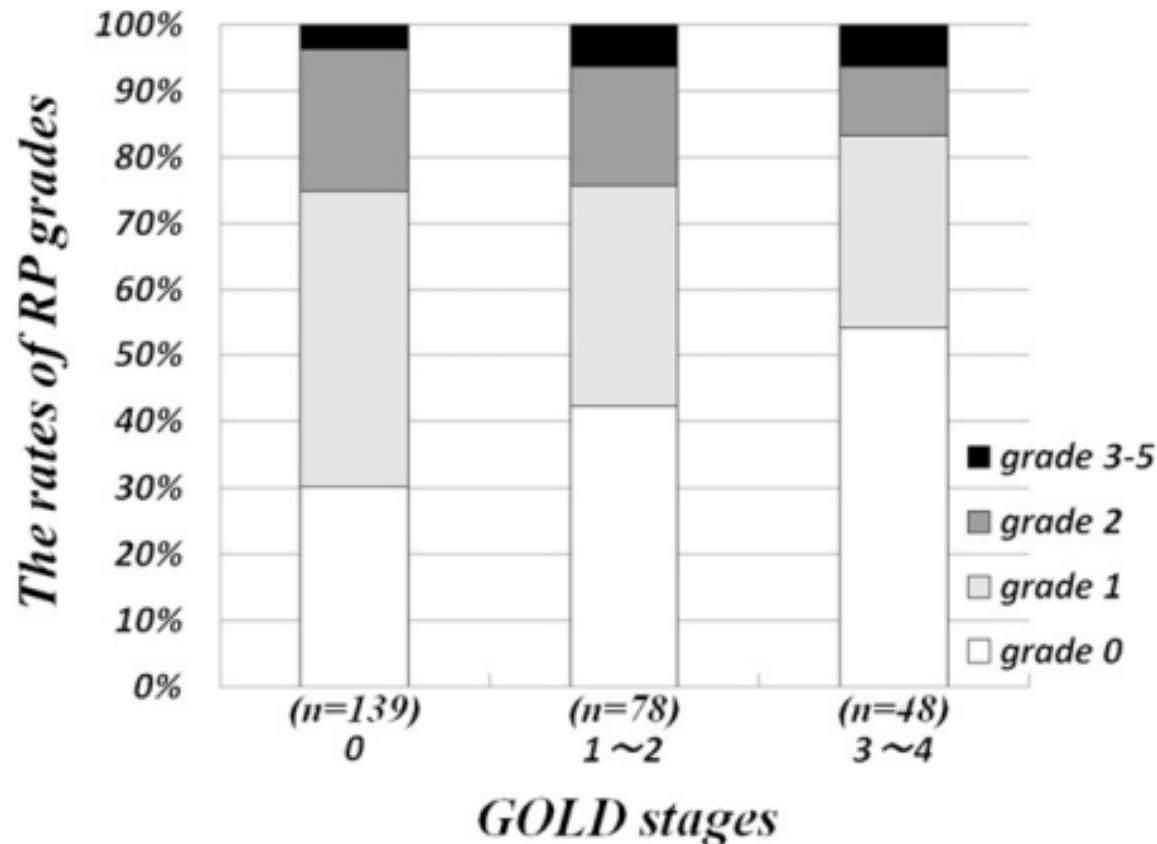
Article

The Value of Residual Volume/Total Lung Capacity as an Indicator for Predicting Postoperative Lung Function in Non-Small Lung Cancer



COPD and Radiation pneumonitis

Severe COPD Is Correlated With Mild Radiation Pneumonitis Following Stereotactic Body Radiotherapy



COPD under ICI treatment

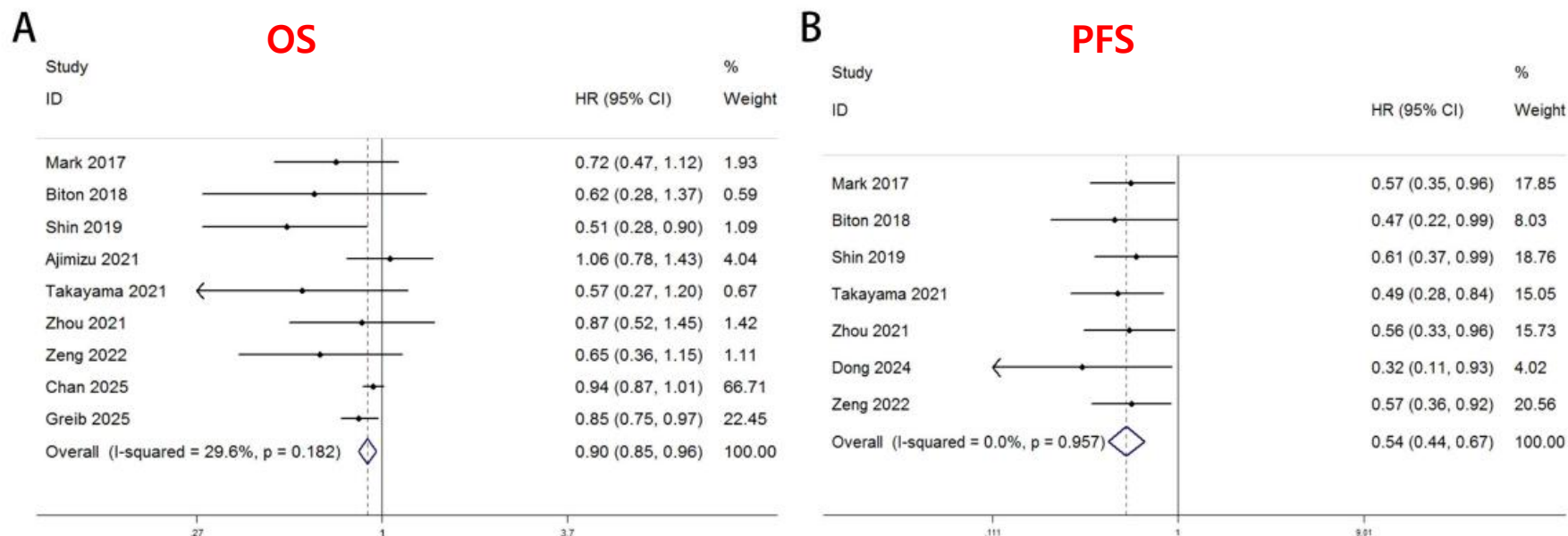
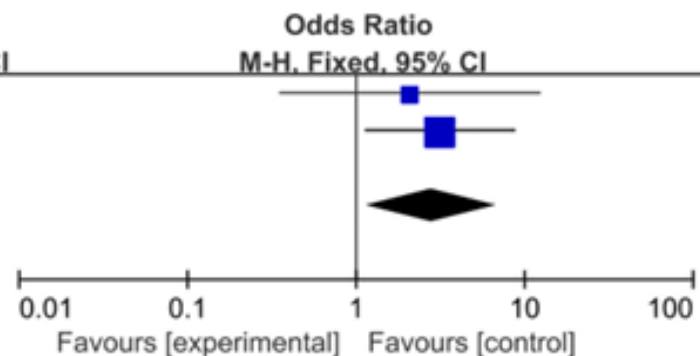


FIGURE 2

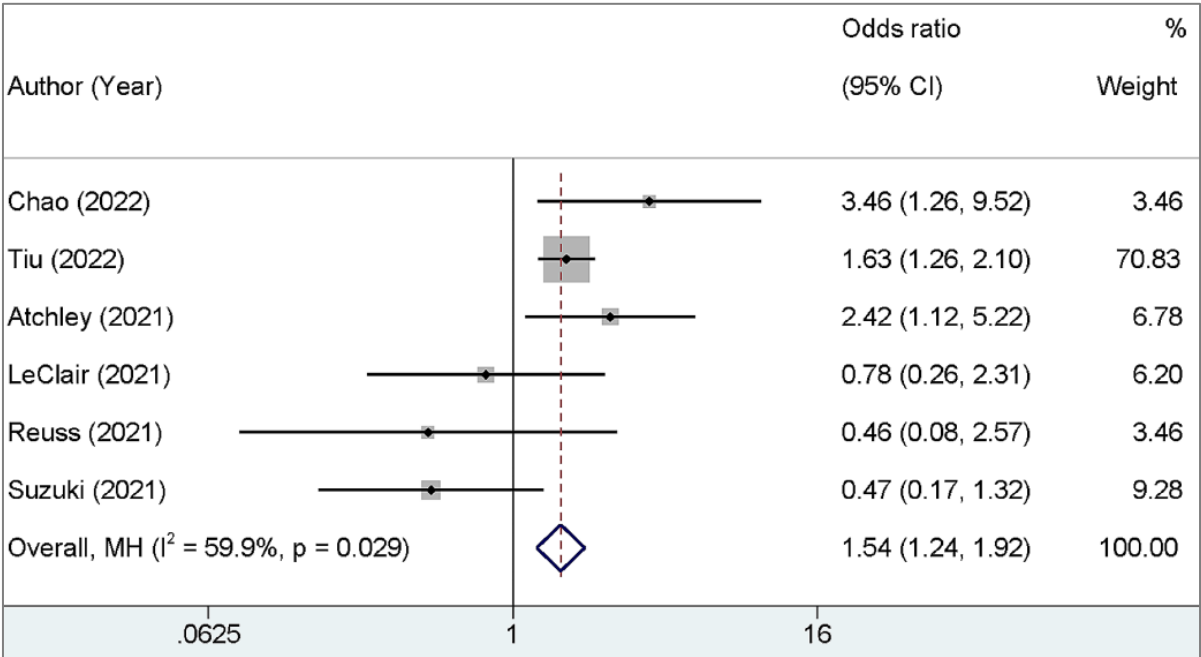
Forest plots delineate the association between COPD and survival outcomes in lung cancer patients treated with ICIs [pOS: (A); PFS: (B)].



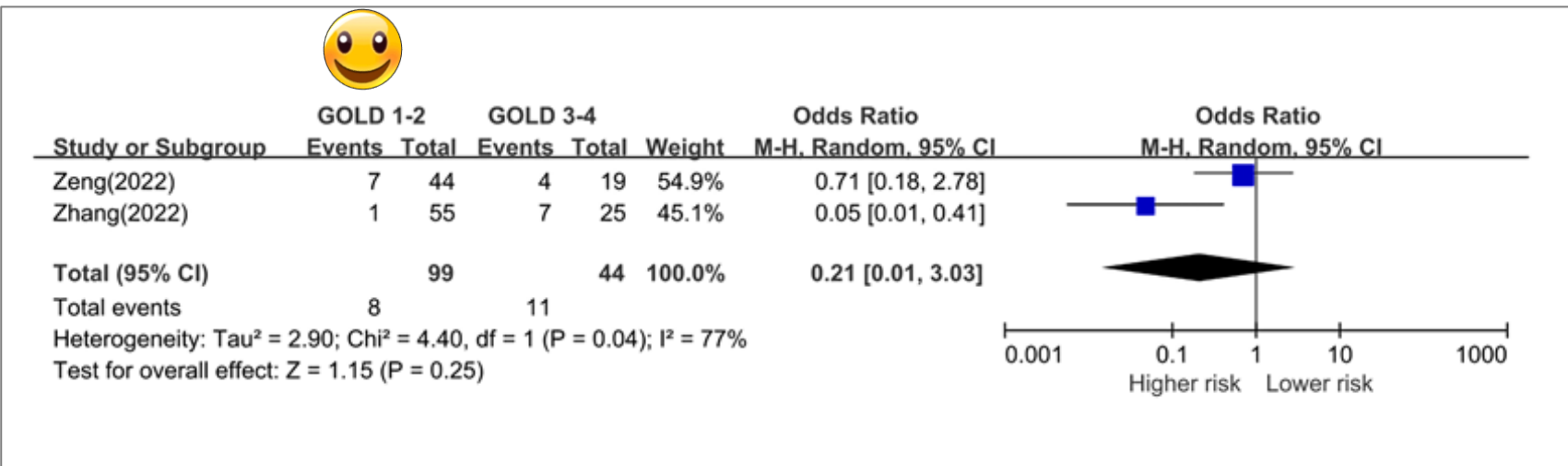
Study or Subgroup	GOLD 1-2		GOLD 3-4		Weight	Odds Ratio M-H, Fixed, 95% CI
	Events	Total	Events	Total		
Shin(2019)	25	49	2	6	31.2%	2.08 [0.35, 12.45]
Zhang(2022)	44	55	14	25	68.8%	3.14 [1.12, 8.80]
Total (95% CI)		104		31	100.0%	2.81 [1.15, 6.89]
Total events	69		16			
Heterogeneity: Chi ² = 0.15, df = 1 (P = 0.70); I ² = 0%						
Test for overall effect: Z = 2.26 (P = 0.02)						



IRP (Immunotherapy-related pneumonitis)



BMC Pulm Med 2024 14;24(1):393



TakeHome Message



특발성 폐섬유증 (IPF)

수술 위험성: 절제술 후 급성 악화(AE) 발생률 7~15%, 30일 사망률 40~70%

고위험

방사선 독성: SBRT 시 폐렴 위험(10~32%). 양성자치료(PBT)로 독성 최소화 (6.3%)

항암제 선택: Carboplatin + weekly Paclitaxel 표준. Docetaxel·Gemcitabine 엄격 금기

항섬유화제 병용: Pirfenidone/Nintedanib을 통한 수술 AE 예방 및 생존기간 연장



만성폐쇄성폐질환 (COPD)

높은 유병률: 폐암 환자의 40~70% 동반, 폐암 발생 위험 2~7배 상승

LVRS 역설 효과: 상업 폐기종 절제(용적감소)로 수술 후 실제 FEV1이 예측치(ppoFEV1) 상회

SBRT 안전성: 과팽창 버퍼 효과로 중증 COPD(GOLD 3-4)도 안전하게 진행 (폐렴률 6.2%)

면역항암제 우수성: 높은 TMB 및 흡연 관련 T세포 활성화로 ICI 치료 효과 증대

높은 반응률