Lung Cancer in Patients with ILD: Diagnostic and Management Considerations

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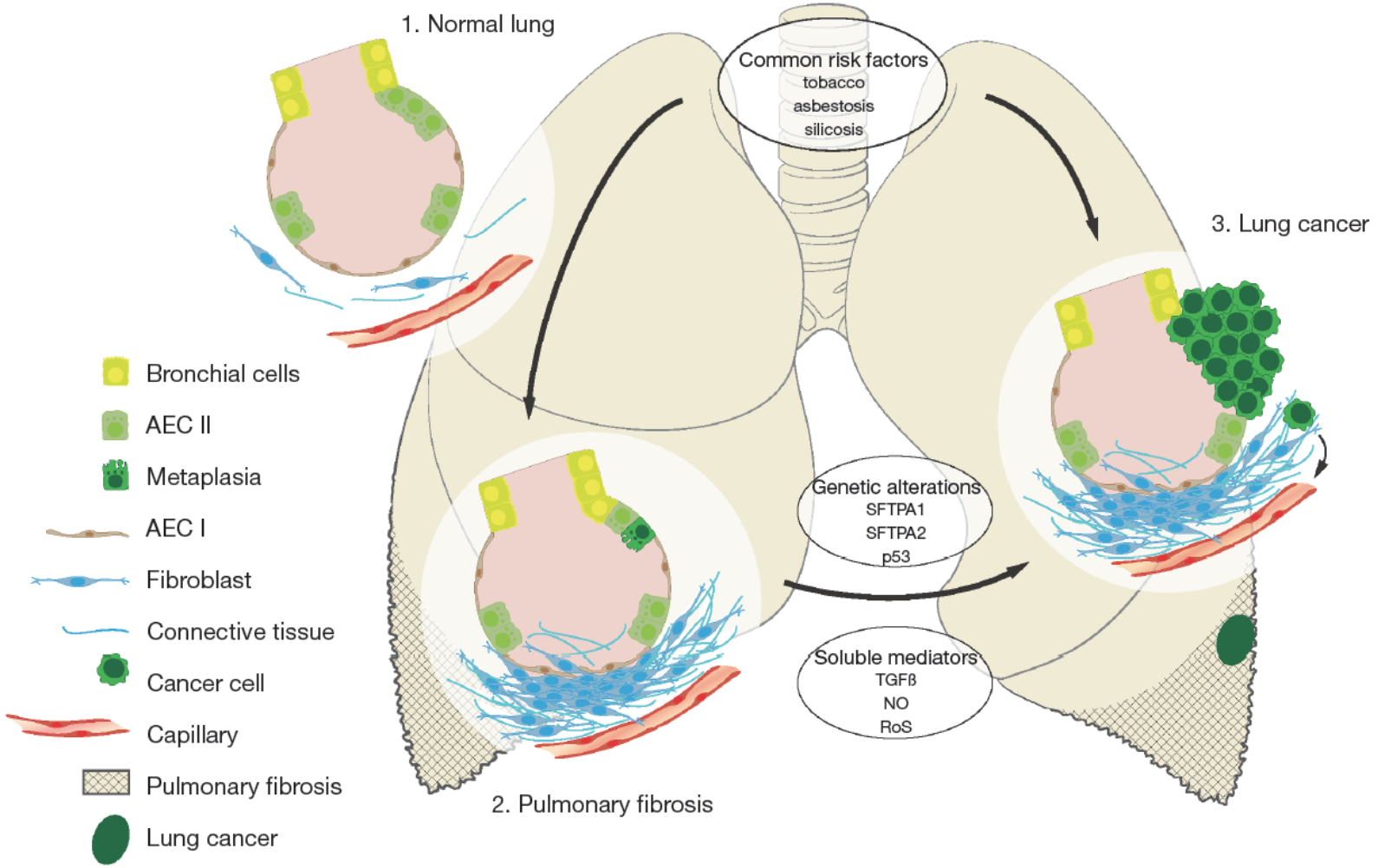
Disclosures

- None

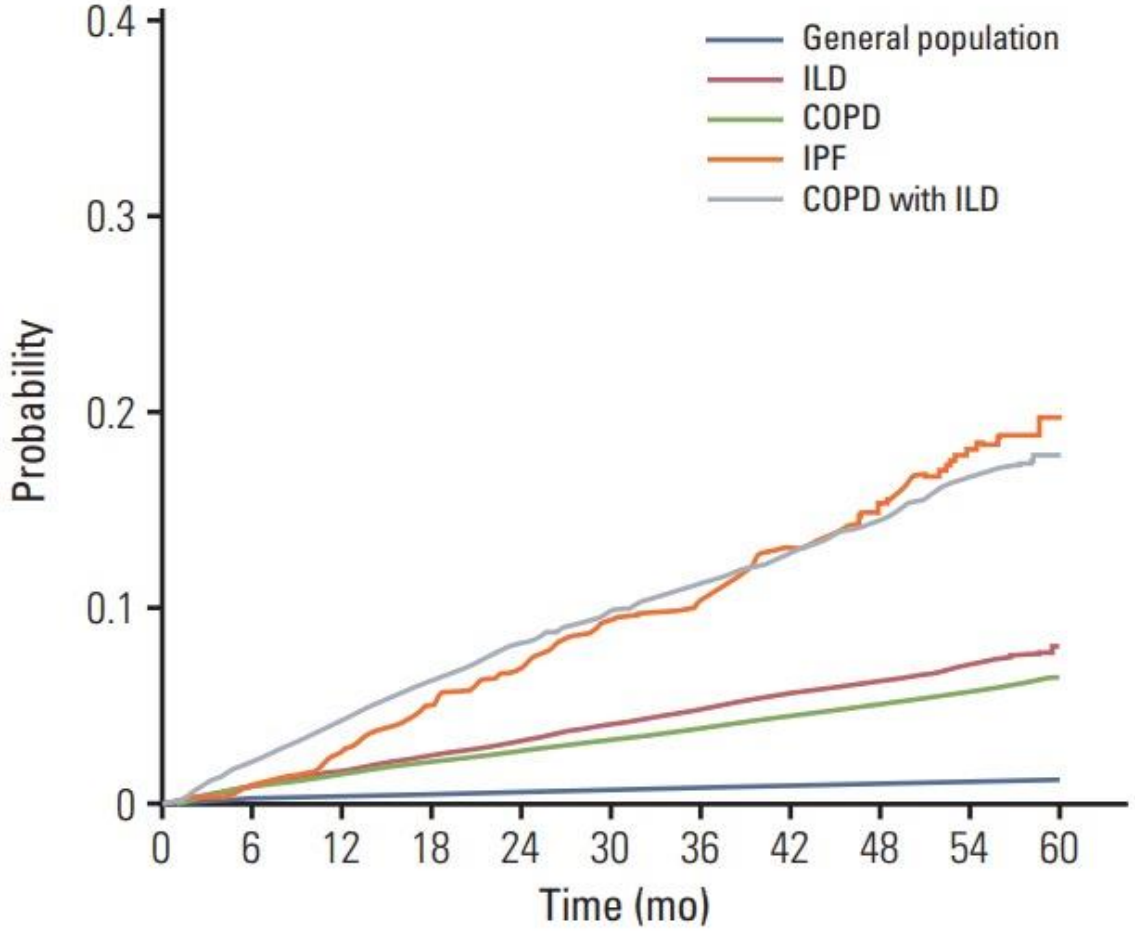
Increased risk of lung cancer in ILD



Naccache et al. J Thorac Dis. 2018;10:3829-3844.

Epidemiology

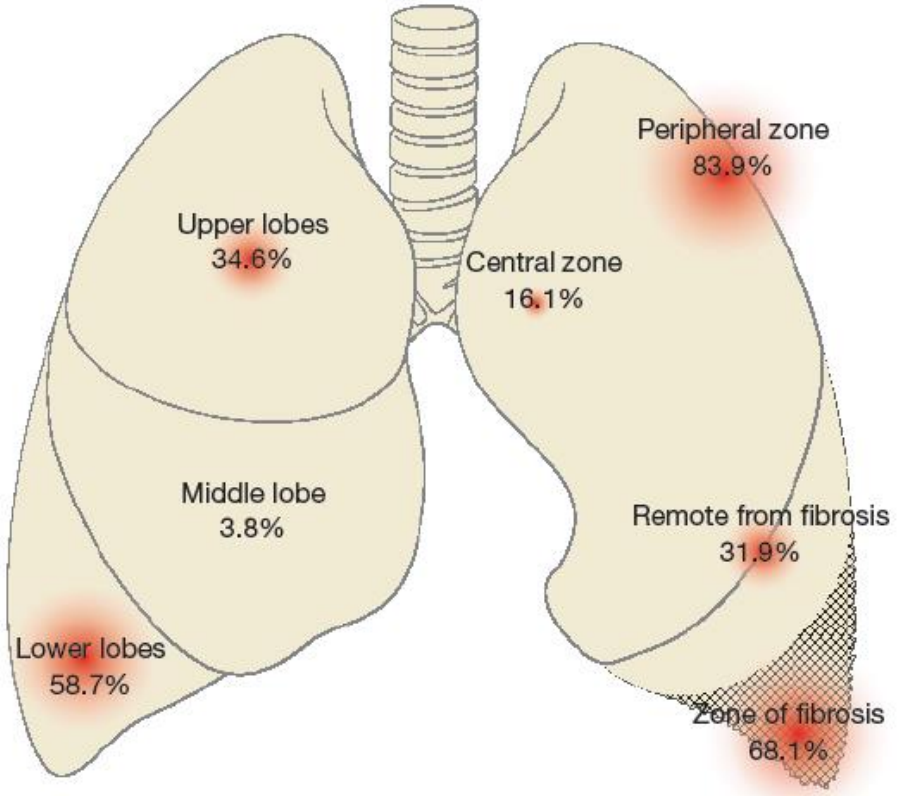
- Estimated 22% of patients with ILD will eventually develop lung cancer
- Estimated prevalence in IPF 13.5%, higher rates in men and smokers
- Higher rates in CTD-ILD vs non-CTD ILD (excluding IPF)
- Most common subtypes:
  - Squamous cell carcinoma (37.8%), adenocarcinoma (30.8%)

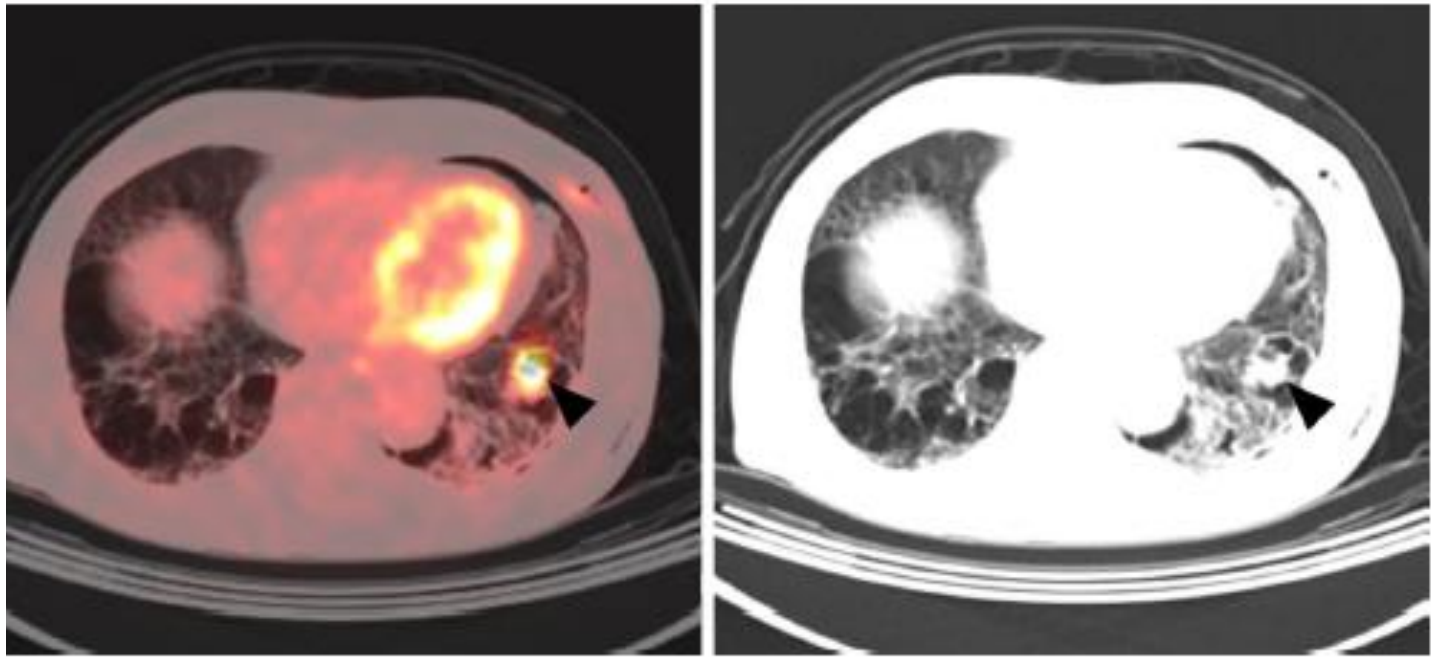


Choi et al. Cancer Res Treat. 2018;50:374-381.

Diagnostic Considerations

- Early detection is important but challenging
- PET/CT demonstrates high sensitivity/specificity in IPF



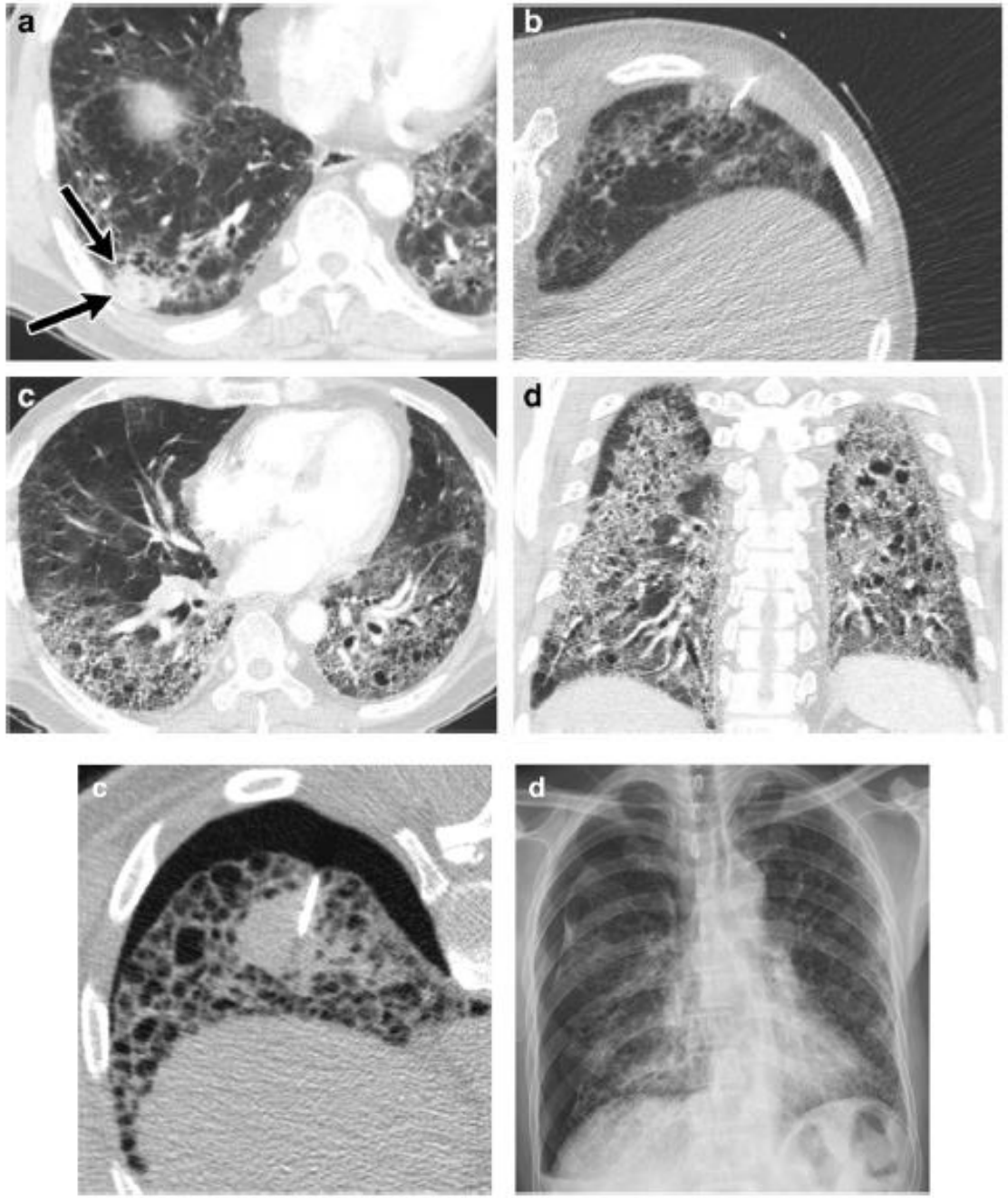


Lee et al. Ann Nuclear Med. 2018;32: 492-498.

Diagnostic Considerations

- CT-guided transthoracic needle biopsy demonstrates high diagnostic accuracy
  - Need to consider relatively high complication rate
    - Acute-exacerbation
    - Pneumothorax requiring chest tube

- Increasing use of advanced bronchoscopic techniques for diagnosis of peripheral lesions



Shin et al. Eur Radiology. 2021;31:9000-9011.

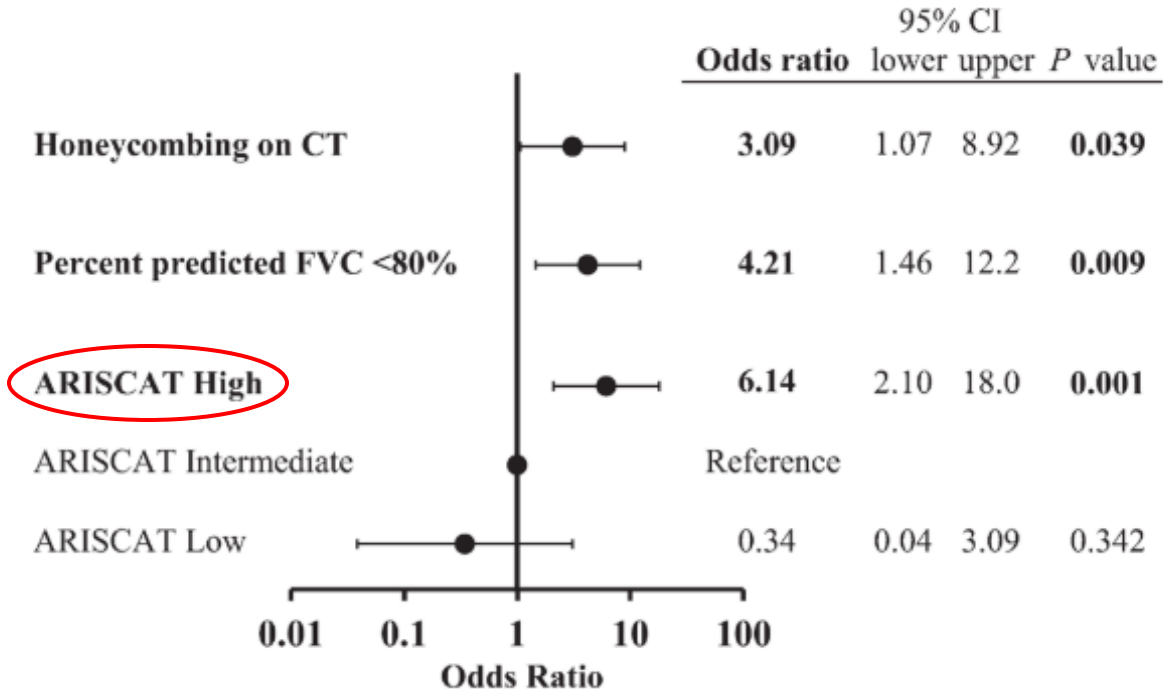
Management Considerations

- Surgical Resection
- Radiation Therapy
- Percutaneous Ablation
- Systemic Therapy
- Immunotherapy

Surgical Resection: Short-term complications

- Increased short-term morbidity and mortality
  - AE-ILD: Incidence 9-23%, median time to onset 2-10 days post-op, high mortality (up to 60%)

- Risk factors:
  - Pulmonary factors
    - Severity of ILD (FVC, DLCO)
    - Pattern of ILD (UIP)
    - ARISCAT score (>45)
  - Procedural-based factors
    - Sublobar vs lobar resection



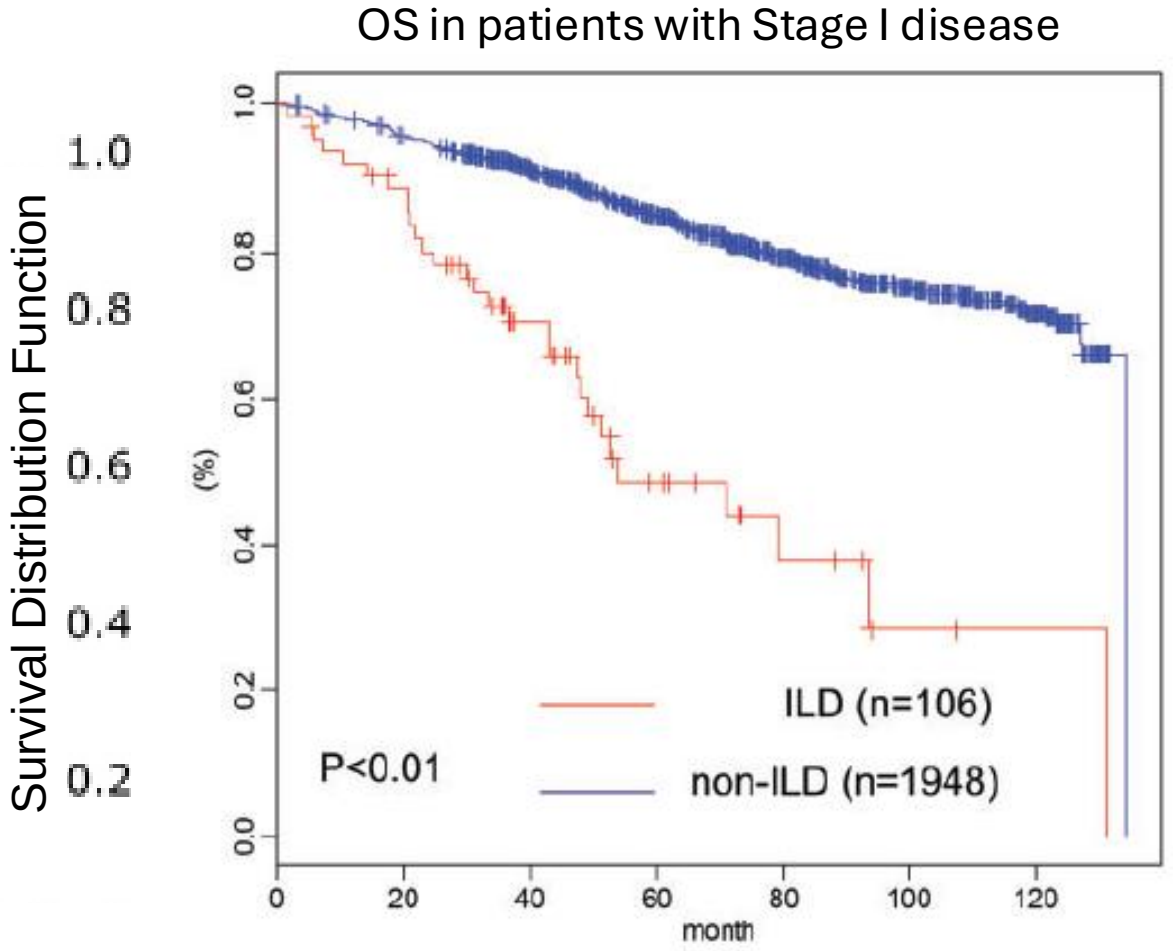
Hosoki et al. BMJ. 2020.
Sato et al. J Thorac Cardiovasc Surg. 2015;149:64-70.
Sato et al. BMC Pulm Med. 2018;18(1):134.

Surgical Resection: Long-term survival

Patients with ILD:

- More likely to undergo limited resection
- Higher frequency of recurrence
- Limited use of systemic therapy w/ recurrence

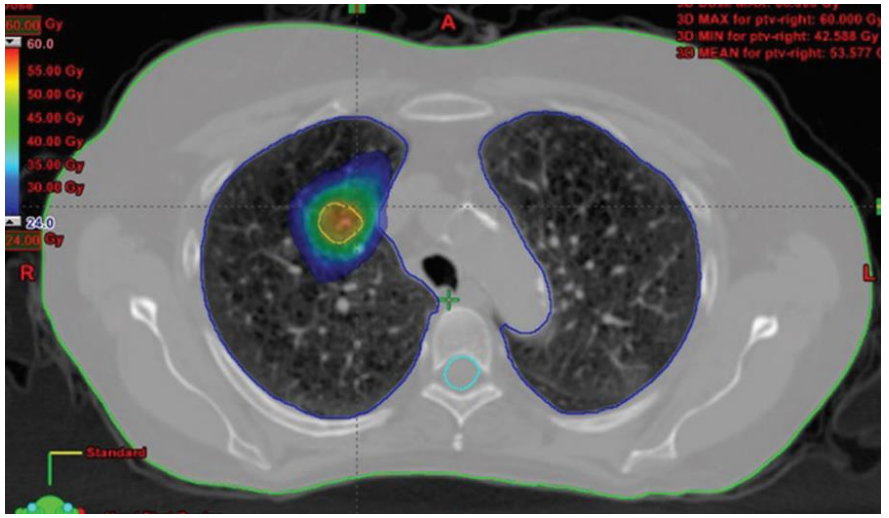
- Main cause of death was lung cancer
  - 5 year OS: 40% vs 72%
  - 5 year OS stage I: 44% vs 85%



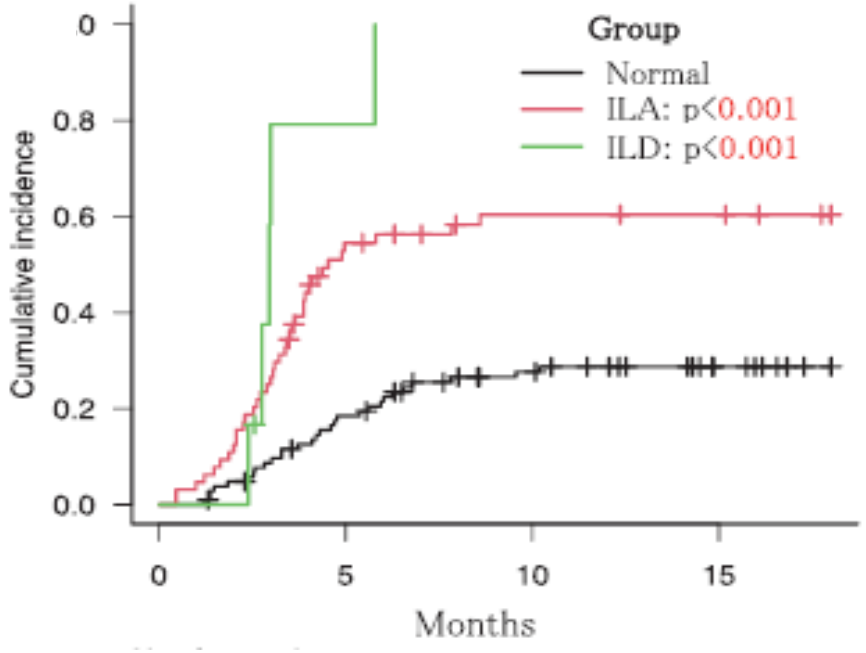
Sekihara et al. Interact Cardiovasc Surg. 2018;26:638-43.
Axtell et al. Ann Thorac Surg. 2023;116:533-42.
Iwata et al. Resp Res. 2016;17:90.

Radiation Therapy

- Standard of care for patients with early-stage NSCLC considered medically inoperable
- Data w/ ILD limited to retrospective studies, significant heterogeneity
- Majority with subclinical, asymptomatic ILD
- Even in pts with subclinical ILD and ILAs, thought to carry significant toxicity



Cumulative incidence of grade ≥2 radiation pneumonitis



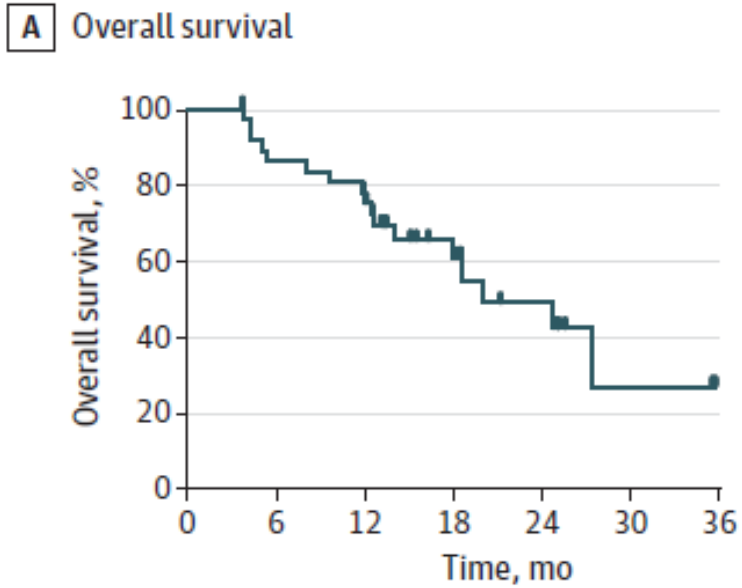
Ito et al. Radiol Oncol. 2023; 57(2):229-38.
Saha et al. Clinical Oncology. 2022; 34:493-504.

Radiation Therapy

ASPIRE-ILD

- 39 pts with pre-existing ILD treated with SABR
- OS at 1 year: 79%; Median OS 25 months
  - Median survival more than double the expected median survival in untreated patients
- Risk of grade 3-5 toxicity half previously reported in prior systemic reviews

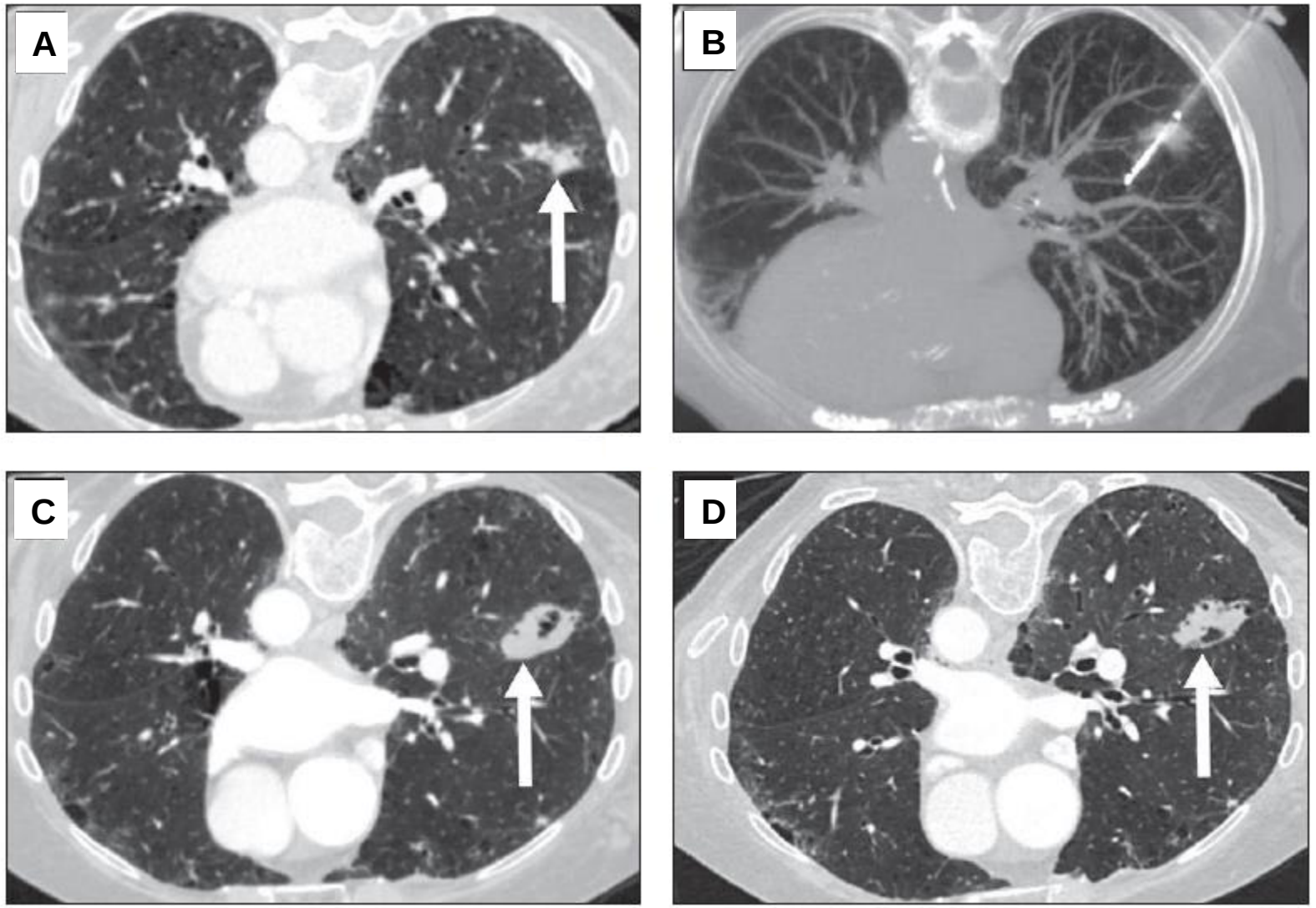
ILD type (multidisciplinary consensus diagnosis), No. (%)	
IPF	8 (21)
NSIP	0
CT-ILD	8 (21)
Chronic HP	2 (5)
Unclassifiable/other	21 (54)
ILD-GAP Index, No. (%)	
≤2	14 (36)
3-5	23 (59)
≥6	2 (5)
Baseline primary tumor size, median (IQR), cm	2.2 (1.6-2.7)
Baseline FEV_1 [% predicted], median (IQR)	80 (66-90)
Baseline FVC [% predicted], median (IQR)	84 (69-94)
Baseline DLCO [% predicted], median (IQR)	49 (38-61)



Palma et al. JAMA Oncol. 2024;10(5):575-582.

Percutaneous ablation

- Safety considerations:
  - Rate of major AE 14%
  - Bronchopleural fistula, pneumothorax, hemothorax, hemoptysis
  - No AE-ILD or death within 90 days
- Outcomes:
  - Local control 78% at 1 year
  - OS 77% at 1 year



Fintelmann et al. AJR 2024;222.

Systemic Therapy

Limited data in this patient population, but first-line platinum doublet therapy for advanced NSCLC shown to be relatively safe and effective

- Pooled ORR 43%, 1 year OS 33%
- Pooled AE-ILD rate 8%

Combination chemo- and radiotherapy increase the risk of pneumonitis in patients with ILD

Rates of AE-ILD shown to be considerably higher with certain second-line agents

	UIP Pattern	
	No. of Patients Administered	Exacerbation of ILD (%)
Cisplatin	21	2 (10)
Carboplatin	40	5 (13)
Paclitaxel	31	1 (3)
Docetaxel	25	7 (28)
Etoposide	21	5 (24)
Vinorelbine	13	0
Gemcitabine	7	3 (43)
S-1	7	2 (29)
Irinotecan	6	2 (33)
Amrubicin	4	0
Pemetrexed	2	1 (50)

Wang et al. Front Oncol. 2020; 10:1636.
Kenmotsu et al. J Thorac Oncol. 2011;6:1242-46.
Otsubo et al. Eur Respir J. 2022;60:2200380.
Reck et al. Lancet Oncol. 2014; 15:143-55.

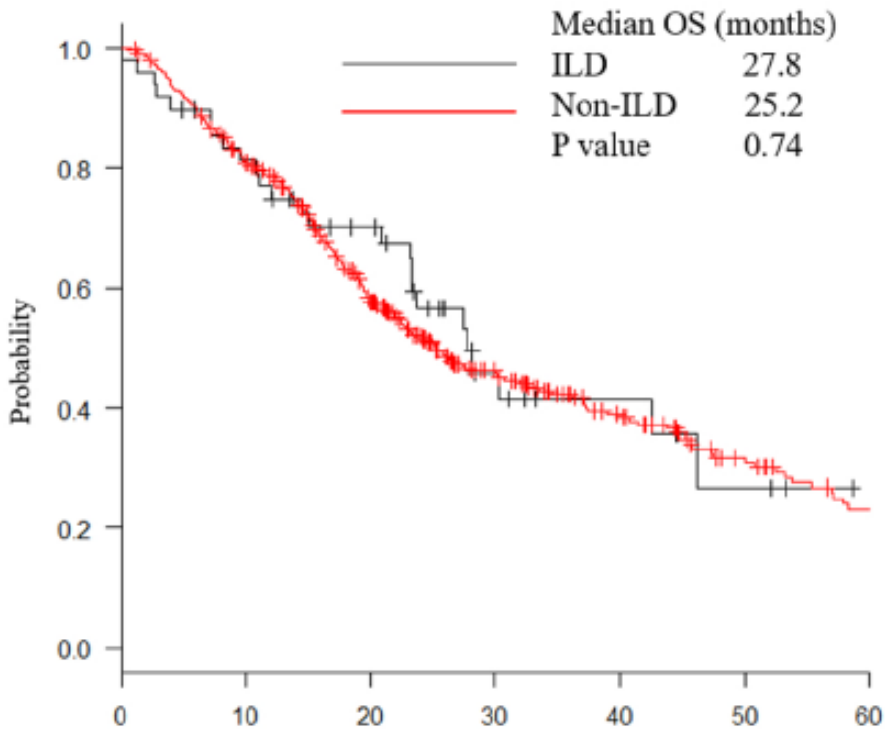
Immunotherapy: Pneumonitis

- Incidence depends on type of treatment:
  - PD-1 inhibitors have ~4-5% reported incidence (maybe higher), PD-L1 inhibitors 2%
  - CTLA-4 inhibitors have ~1% incidence
  - Combination PD-1/CTLA-4 treatment associated with 10% incidence
- Median time to onset is ~3 months, however wide range (2-24 months) and can occur months after discontinuation
- 1/3 of patients present as ≥ grade 3, fatal in up to 12% of patients
- Up to 14% may develop steroid-dependent pneumonitis, 19% steroid-refractory pneumonitis
- Recurrent pneumonitis is frequent – both spontaneous and with rechallenge

Cho JY et al. Lung Cancer. 2018 Nov;125:150-156.
Suresh K et al. J Thorac Oncol. 2018 Dec;13(12):1930-1939
Daetwyler et al. *J Immunother Cancer*. 2024;12:e007409

Immunotherapy: Pre-existing ILD

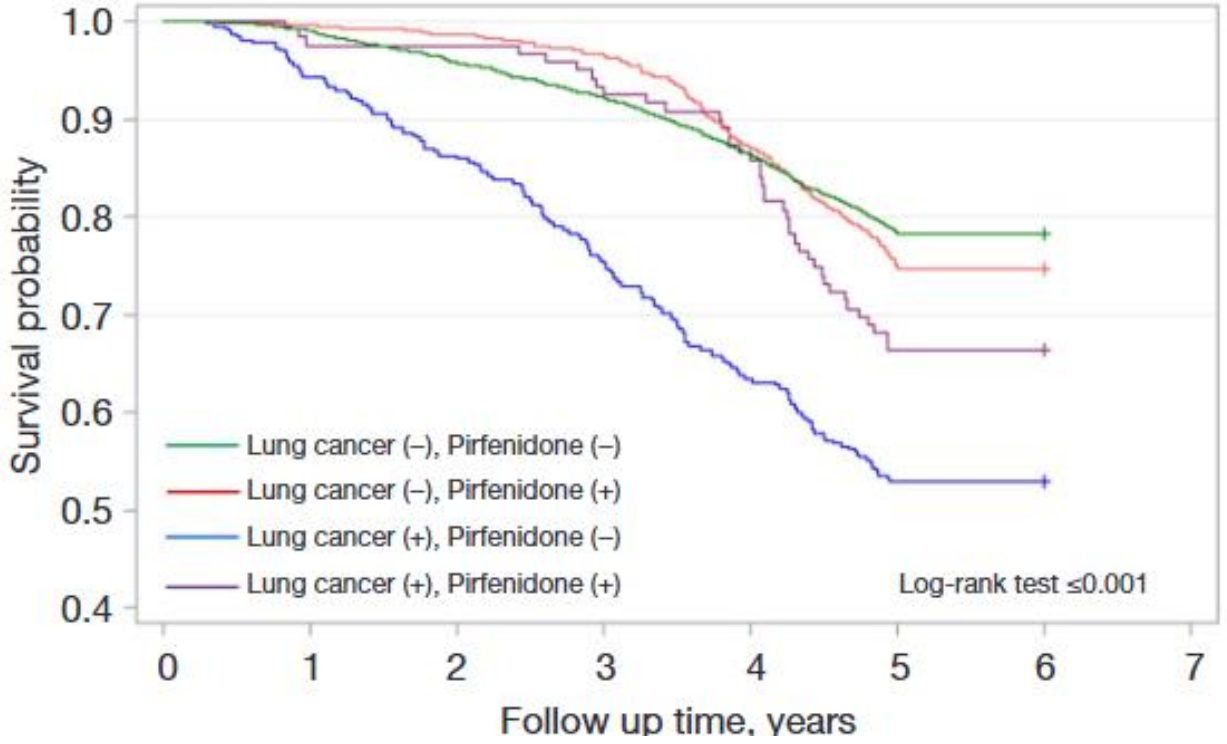
- Increased risk of pneumonitis
  - Incidence of all grade pneumonitis 27% vs 10%
  - Incidence of >grade 3 pneumonitis 15% vs 4%
- Non-inferior outcomes
  - Majority improve upon ICI discontinuation +/- corticosteroid administration
  - Similar disease control rates, progression free survival, overall survival
- Patients need to be informed and closely monitored
  - Can we better risk stratify these patients?
    - Radiographic pattern, severity of ILD



Zhang et al. *CHEST*. 2022; 161(6):1675-1686
Tasaka et al. *Lung Cancer.* 2021; 155:120-126

Role of antifibrotics

- Reduction in post-operative AE-IPF
- Treatment of radiation pneumonitis
- Combination with chemotherapy
- Reduce risk of ICI-pneumonitis



Iwata et al. Resp Res. 2016;17:90
Jo et al. J Thorac Dis. 2024;16(12):8528-8537.
Rimner et al. Int J Radiat Oncol. 2023;116:1091-1099.

Summary

- Patients with ILD are at increased risk for lung cancer
- Diagnosis is complex due to underlying parenchymal abnormalities
- Regardless of treatment, patients with ILD experience higher treatment-related morbidity and mortality
  - Major concern AE-ILD
- Patients with ILD require multidisciplinary evaluation to determine a personalized treatment plan tailored to their goals of care