SDB and interstitial lung diseases

일산백병원 호흡기내과 강지은

Contents

- Sleep characteristics in ILD
- Prevalence
- Pathophysiological relationship between OSA and ILDs
- Clinical presentation and PSG characteristics
- Clinical outcomes
- Screening and diagnosis
- Treatment

Contents

- Sleep characteristics in ILD
- Prevalence
- Pathophysiological relationship between OSA and ILDs
- Clinical presentation and PSG characteristics
- Clinical outcomes
- Screening and diagnosis
- Treatment

Sleep characteristics in ILD

Poor sleep quality in patients with ILD compared to the normal population

- disturbed sleep architecture
- frequent arousals and sleep fragmentation
- nocturnal hypoxemia

Sleep changes in ILD

- affect sleep quality and contribute to daytime fatigue

Mermigkis C et al. Chest 2017

Sleep characteristics in ILD

Characteristics	Abnormality	Patient group
Respiratory rate	Unchanged Decreased	ILD, IPF ILD
Stage 1,2 sleep	Increased	ILD IPF
REM sleep	Reduced	ILD Scleroderma IPF
Slow wave sleep	Reduced	ILD IPF
Arousal index	Increased	ILD IPF
Sleep efficiency	Reduced	ILD IPF

Sleep characteristics in ILD

ILD patients have **<u>rapid, shallow breathing pattern</u>**

- Increased elastic loading of respiratory muscles
- Stimulation of peripheral mechanoreceptors

Maintain eucapnia until very advanced stage

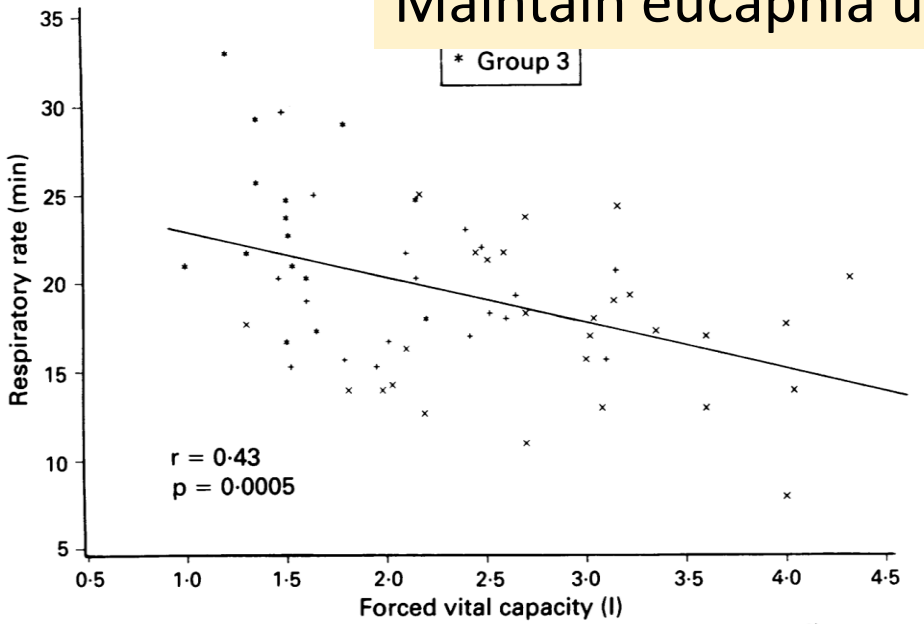


Figure 1 Linear regression between forced vital capacity (FVC) and respiratory rate (RR).

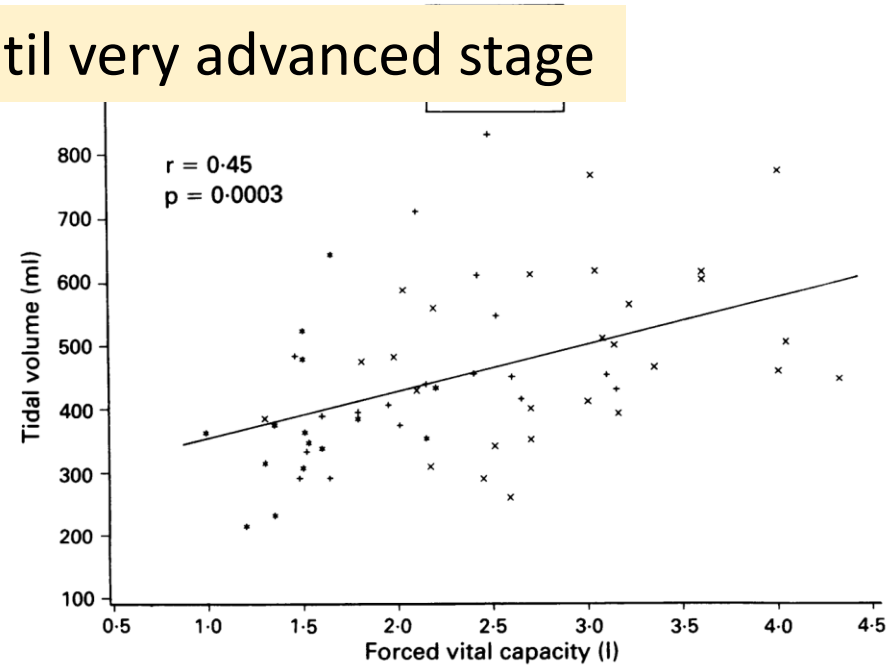


Figure 2 Linear regression between forced vital capacity and tidal volume (V_T).

Javaheri S et al. Thorax 1992

Sleep characteristics in ILD

Characteristics	Abnormality	Patient group
Respiratory rate	Unchanged Decreased	ILD, IPF ILD
Stage 1,2 sleep	Increased	ILD IPF
REM sleep	Reduced	ILD Scleroderma IPF
Slow wave sleep	Reduced	ILD IPF
Arousal index	Increased	ILD IPF
Sleep efficiency	Reduced	ILD IPF

Contents

- Sleep characteristics in ILD
- Prevalence
- Pathophysiological relationship between OSA and ILDs
- Clinical presentation and PSG characteristics
- Clinical outcomes
- Screening and diagnosis
- Treatment

Prevalence

Prevalence of OSA in IPF patients markedly exceed that reported in healthy age-matched populations

- **41-90%** depending on the population studied

OSA prevalence seems to be **higher in IPF than other ILDs**

Mermigkis C et al. Chest 2017
Schiza SE et al. Curr Opin Pulm Med 2020

Prevalence

Reference	Population	Prevalence	Age	Included patients
Mermigkis 2007	IPF	11/18 (61%)	68.1	Retrospective study; patients with symptoms of SDB Type 1 PSG
Lancaster 2009	IPF	44/50 (88%)	64.9	Unselected patients Type 1 PSG
Mermigkis 2010	IPF	20/34 (59%)	65.0	Newly diagnosed IPF Type 1 PSG
Kolilekas 2013	IPF	28/31 (90%)	68.0	Newly diagnosed IPF Type 1 PSG
Pihtili 2013	Overall IPF Sarcoidosis Scleroderma	34/50 (68%) 14/17 (82%) 10/15 (67%) 10/18 (56%)	53.9	Prospective study; excluded obese subjects (BMI ≥ 30) Type 1 PSG
Mermigkis 2015	IPF	78/92 (85%)	70.3	Newly diagnosed IPF Type 1 PSG
Bosi 2017	IPF	25/35 (71%)	68.2	Room air breathing IPF outpatient Type 2 PSG
Gille 2017	IPF	40/45 (89%)	68.8	Newly diagnosed IPF

Prevalence

Reference	Population	Prevalence	Age	Included patients
Mavroudi 2017	Overall IPF Sarcoidosis II/III	17/41 (41%) 15/19 (79%) 12/21 (52%)	 69.8 53.8	Prospective study Type 1 PSG
Pereira 2019	Overall IPF CTD-ILD CHP Sarcoidosis IV PPFE Vasculitis	34/49 (70%) 10/12 (83%) 7/10 (70%) 16/21 (76%) 1/4 (25%) 0/1 (0%) 0/1 (0%)	67.2	49 patients with FLD and BMI less than 30 Type 3 PSG

American Thoracic Society Documents

An Official ATS/ERS/JRS/ALAT Statement: Idiopathic Pulmonary Fibrosis: Evidence-based Guidelines for Diagnosis and Management

AMERICAN THORACIC SOCIETY DOCUMENTS

Diagnosis of Idiopathic Pulmonary Fibrosis
An Official ATS/ERS/JRS/ALAT Clinical Practice Guideline

AMERICAN THORACIC SOCIETY DOCUMENTS

Idiopathic Pulmonary Fibrosis (an Update) and Progressive Pulmonary Fibrosis in Adults
An Official ATS/ERS/JRS/ALAT Clinical Practice Guideline

Sleep apnea as a common comorbidity in IPF

Raghu H et al. AJRCCM 2011
Raghu H et al. AJRCCM 2018
Raghu H et al. AJRCCM 2022

Prevalence

RESEARCH ARTICLE

Obstructive sleep apnea in patients with interstitial lung disease: Prevalence and predictive factors

Jae Ha Lee[1], Chan Sun Park[2], Jin Woo Song[3]*

1 Division of Pulmonology, Department of Internal Medicine, Inje University Haeundae Paik Hospital, Inje University College of Medicine, Busan, Republic of Korea, **2** Division of Allergy, Department of Internal Medicine, Inje University Haeundae Paik Hospital, Inje University College of Medicine, Busan, Republic of Korea, **3** Department of Pulmonary and Critical Care Medicine, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea

Retrospective analysis of 86 patients who underwent respiratory polygraphy (level IV)

Variable	Overall	OSA 53.5%	No OSA	P-value
Patient, No.	86	46	40	
IPF	57 (66.3)	37 (80.4)	20 (50.0)	0.004
NSIP	5 (5.8)	2 (4.3)	3 (7.5)	
CTD	14 (16.3)	4 (8.7)	10 (25.0)	
COP	5 (5.8)	0 (0.0)	5 (12.5)	
HP	4 (4.7)	3 (6.5)	1 (2.5)	

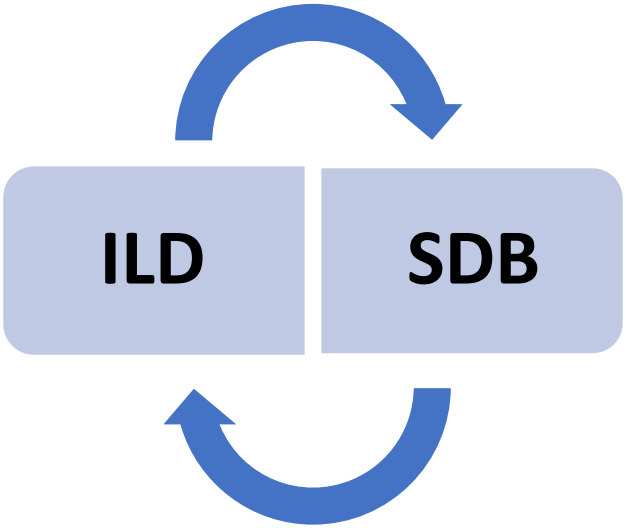
Lee JH et al. PLos One 2020

Contents

- Sleep characteristics in ILD
- Prevalence
- Pathophysiological relationship between OSA and ILDs
- Clinical presentation and PSG characteristics
- Clinical outcomes
- Screening and diagnosis
- Treatment

Pathophysiological relationship

Why SDB is increased in patients with ILD?



Does OSA contribute to ILD?

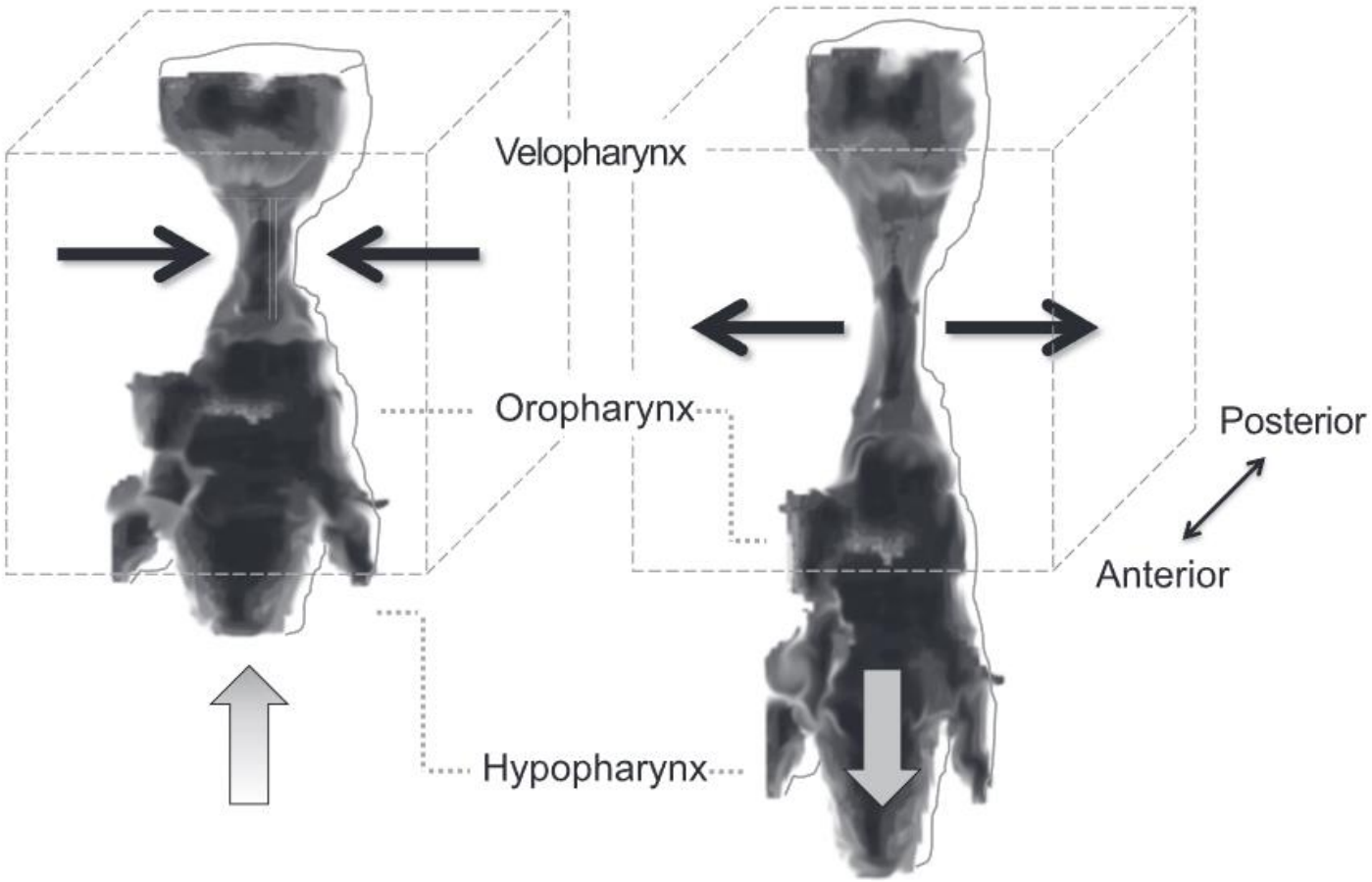
Pathophysiological relationship

Why SDB is increased in patients with ILD?

1) Upper airway collapsibility

ILD (characterized by reduced lung volume)
→ Reduce upper airway stability and increase resistance due to reduced caudal taction of upper airway
→ Especially during REM sleep as FRC is further reduced

Khor YH et al. Sleep Medicine Reviews 2021
Bouloukaki I et al. Breath 2022



Schwartz AR et al. J Appl Physiol 2012
Schwab RJ et al. Am J Respir Crit Care Med 2003

Pathophysiological relationship

Why SDB is increased in patients with ILD?

1) Upper airway collapsibility

ILD (characterized by reduced lung volume)
→ Reduce upper airway stability and increase resistance due to reduced caudal taction of upper airway
→ Especially during REM sleep as FRC is further reduced

Q. Inverse correlation between lung volume and AHI ??

Khor YH et al. Sleep Medicine Reviews 2021
Bouloukaki I et al. Breath 2022

Pathophysiological relationship

Why SDB is increased in patients with ILD?

2) Ventilatory control system instability

Chronic hypoxia
→ Enhance chemoreceptor responsiveness, exacerbating ventilatory instability in susceptible individuals

Khor YH et al. Sleep Medicine Reviews 2021
Bouloukaki I et al. Breath 2022

Pathophysiological relationship

Why SDB is increased in patients with ILD?

3) Respiratory arousal threshold

Increased work of breathing during sleep secondary to respiratory loading may cause patients to reach arousal threshold more often

Khor YH et al. Sleep Medicine Reviews 2021

Pathophysiological relationship

Does OSA contribute to ILD?

1) Repetitive forced inspirations against a closed airway

Breathing against a closed upper airway may lead to alveolar injury via local traction

During apneas and hypopneas

→ Swings in pleural pressures, resulting in regional alveolar pressure differences

→ Repetitive local tractional stress and stretch on alveolar epithelium which can cause alveolar cellular injury and inflammation

Adegunsoye A et al. Chest 2020
Bouloukaki I et al. Breath 2022

Pathophysiological relationship

Does OSA contribute to ILD?

2) Gastroesophageal reflux

OSA is associated with increased nocturnal gastroesophageal reflux
- negative pleural pressure and subsequent raised transdiaphragmatic pressure facilitates reflux of gastric contents into the esophagus

GERD → contributing or a disease modifying factor in ILD

Adegunsoye A et al. Chest 2020
Khor YH et al. Sleep Medicine Reviews 2021
Bouloukaki I et al. Breath 2022

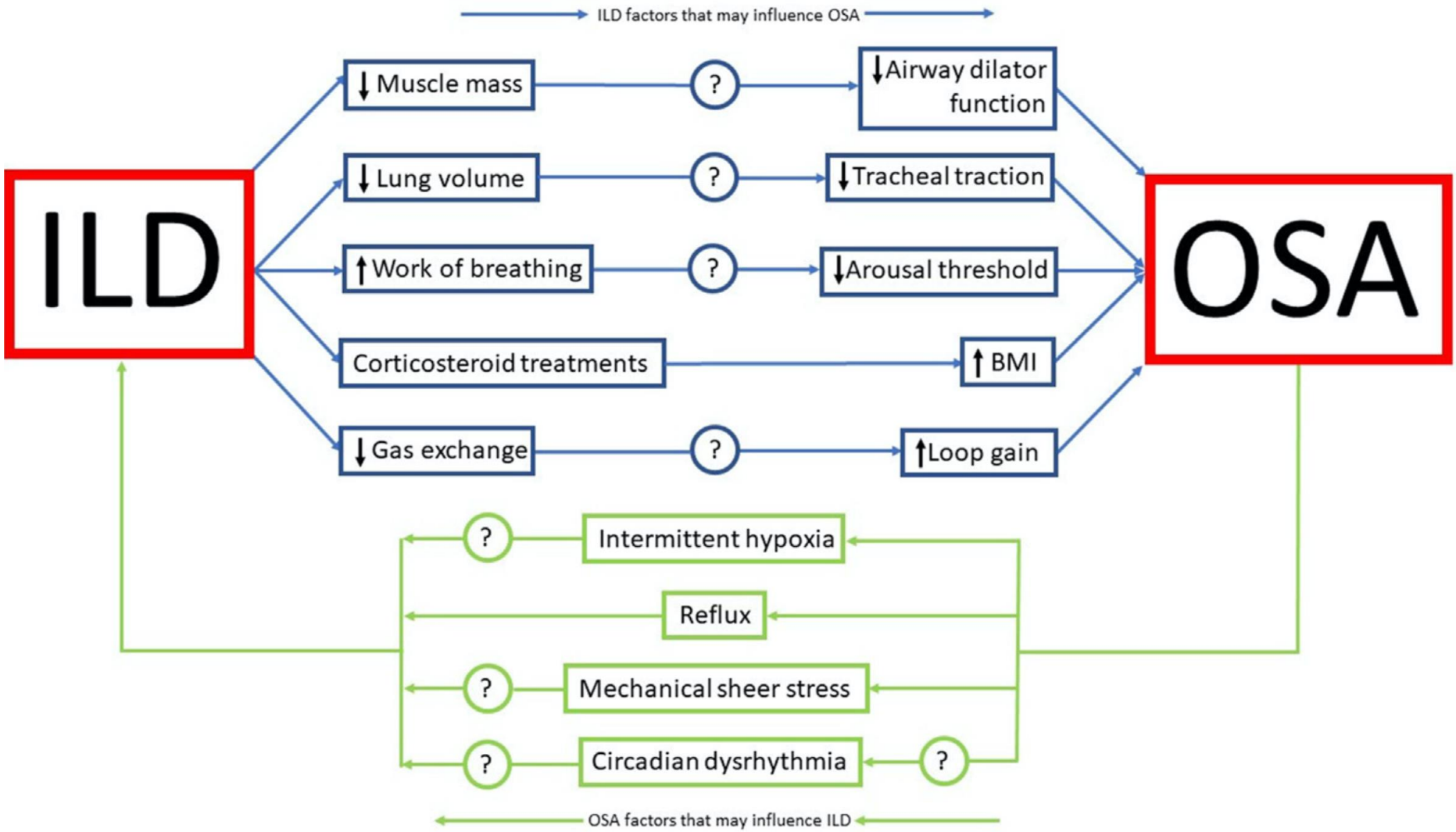
Pathophysiological relationship

Does OSA contribute to ILD?

3) Intermittent hypoxia

Induce oxidative stress with accumulation of reactive oxygen species in lung tissues and systemic circulation

Adegunsoye A et al. Chest 2020
Khor YH et al. Sleep Medicine Reviews 2021
Bouloukaki I et al. Breath 2022



Khor YH et al. Sleep Medicine Reviews 2021

ORIGINAL RESEARCH

Obstructive Sleep Apnea and Subclinical Interstitial Lung Disease in the Multi-Ethnic Study of Atherosclerosis (MESA)

John S. Kim[1]*, Anna J. Podolanczuk[1]*, Priya Borker[2], Steven M. Kawut[3], Ganesh Raghu[4], Joel D. Kaufman[4,5], Karen D. Hinckley Stukovsky[6], Eric A. Hoffman[7], R. Graham Barr[1,8], Daniel J. Gottlieb[9,10], Susan S. Redline[2,9]*, and David J. Lederer[1,8]*

MESA cohort

→ Prospective cohort designed to investigate subclinical cardiovascular disease

→ Patients with polysomnography + HRCT (n = 1152)

Kim JS et al. Ann ATS 2017

	Mean Percent HAA Increment Compared with oAHI < 5 Events/h (95% CI)			
	<5 Events/h	5–15 Events/h	>15 Events/h	*P* Trend
Precision adjusted	0 (Ref)	1.4 (–1.2 to 3.9)	7.2 (4.5 to 10)	<0.001
Adjusted	0	0.2 (–0.2 to 2.7)	4.0 (1.4 to 6.8)	0.001
Adjusted with BMI interaction terms				
<25 kg/m^2	0	4.7 (0.1 to 9.5)	6.1 (0.5 to 12.0)	0.03
25–30 kg/m^2	0	−1.9 (–5.6 to 2.0)	0.8 (–3.2 to 5.1)	0.48
>30 kg/m^2	0	−3.1 (–7.5 to 1.5)	2.7 (–1.6 to 7.3)	0.03
Adjusted with smoking interaction term				
Never-smokers	0	3.5 (–0.01 to 7.4)	9.6 (5.6 to 13.6)	<0.001
Ever-smokers	0	0.3 (–3.0 to 3.8)	5.2 (1.6 to 8.9)	0.002

	Odds Ratio for ILA Compared with oAHI < 5 Events/h (95% CI)		
<5 Events/h	5–15 Events/h	>15 Events/h	*P* Trend
1 (Ref)	1.32 (0.87 to 2.00)	1.64 (1.36 to 1.98)	<0.001
1	0.96 (0.62 to 1.51)	1.35 (1.13 to 1.61)	<0.001
1	2.06 (1.16 to 3.6)	2.31 (1.30 to 4.12)	0.005
	0.71 (0.35 to 1.43)	0.51 (0.23 to 1.12)	0.10
	0.77 (0.29 to 2.07)	1.82 (1.13 to 2.93)	<0.001
1	0.73 (0.32 to 1.64)	1.38 (0.84 to 2.28)	0.01
1	1.33 (0.75 to 2.35)	1.50 (0.99 to 2.27)	0.050

Adjusted for age, sex, race, educational attainment, height, smoking status, cigarette pack-years, glomerular filtration rate, study site, percent emphysema, radiation dose, and total volume of imaged lung

Kim JS et al. Ann ATS 2017

	Mean Percent HAA Increment Compared with a Saturation ⩾ 90% (95% CI)			
	<80%	80–89%	⩾90%	*P* Trend
Precision adjusted	6.1 (2.6 to 9.8)	3.8 (0.9 to 6.8)	0 (Ref)	0.003
Adjusted	4.6 (1.3 to 8.0)	2.4 (–0.4 to 5.2)	0	0.01
Adjusted with BMI interaction term				
<25 kg/m^2	6.9 (–0.1 to 14.3)	3.1 (–1.1 to 7.5)	0	0.049
25–30 kg/m^2	−0.5 (–5.7 to 4.9)	2.1 (–2.4 to 6.8)	0	0.79
>30 kg/m^2	2.6 (–4.1 to 9.8)	−1.8 (–8.0 to 4.8)	0	0.03
Adjusted with smoking interaction term				
Never-smokers	8.1 (3.3 to 13.2)	4.4 (0.4 to 8.6)	0	0.002
Ever-smokers	9.0 (4.2 to 14.1)	5.1 (1.0 to 9.4)	0	0.001

	Odds Ratio for ILA Compared with a Saturation ⩾ 90% (95% CI)			
	<80%	80–89%	⩾90%	*P* Trend
	1.64 (1.23 to 2.17)	1.21 (0.92 to 1.61)	1 (Ref)	<0.001
	1.35 (0.86 to 2.11)	1.09 (0.76 to 1.58)	1	0.08
	0.71 (0.14 to 3.60)	2.02 (0.93 to 4.41)	1	0.59
	0.86 (0.28 to 2.62)	0.70 (0.28 to 1.76)	1	0.95
	1.89 (0.48 to 7.41)	1.31 (0.27 to 6.30)	1	0.003
	0.97 (0.50 to 1.89)	0.98 (0.40 to 2.37)	1	0.93
	2.29 (1.08 to 4.82)	1.51 (0.72 to 3.16)	1	0.008

Kim JS et al. Ann ATS 2017

SP-A: alveolar epithelial injury
MMP-7: fibrogenesis and extracellular remodeling

	Mean Percent Biomarker Increment*	95% CI	*P* Value	*P* for Interaction with BMI
Obstructive AHI				
MMP-7				<0.001
Overall	3.4	0.8 to 6.0	0.01	
BMI < 25	16.6	9.7 to 24.0	<0.001	
BMI > 25	1.6	−0.9 to 4.1	0.21	
SP-A				0.03
Overall	4.1	−0.5 to 8.9	0.08	
BMI < 25	17.5	4.5 to 32.2	0.008	
BMI > 25	1.7	−3.0 to 6.6	0.48	
Nadir Saturation				
MMP-7				0.19
Overall	4.2	−0.4 to 9.0	0.07	
BMI < 25	15.0	−0.8 to 33.2	0.06	
BMI > 25	3.6	−1.2 to 8.7	0.15	
SP-A				0.15
Overall	9.1	0.8 to 18.1	0.03	
BMI < 25	22.8	−5.3 to 59.1	0.12	
BMI > 25	6.4	−2.2 to 15.7	0.15	
Central Sleep Apnea Index				
MMP-7				0.93
Overall	6.8	−3.8 to 18.5	0.21	
BMI < 25	5.4	−8.1 to 21.0	0.45	
BMI > 25	6.4	−9.0 to 24.4	0.43	
SP-A				0.95
Overall	−2.7	−19.4 to 17.5	0.77	
BMI < 25	0.8	−21.0 to 28.7	0.95	
BMI > 25	−0.4	−24.5 to 31.5	0.98	

*Adjusted mean percent increment in each biomarker per 5-unit absolute increase in obstructive AHI, 5% absolute decrement in nadir saturation, or 1-unit increase in central sleep apnea index.

Kim JS et al. Ann ATS 2017

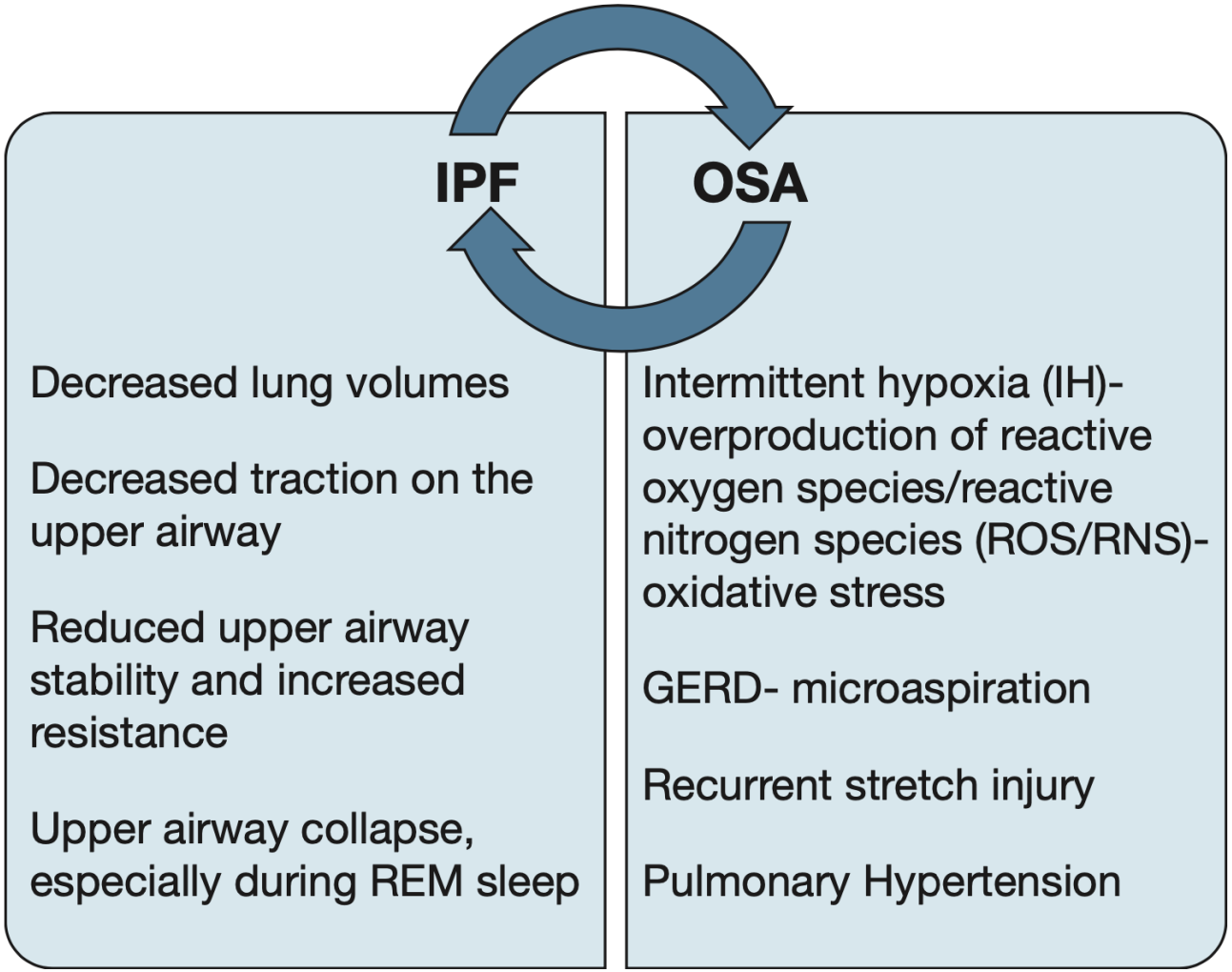


Figure 1 – *Possible pathophysiologic pathways connecting IPF and OSA. GERD = gastroesophageal reflux disease; IPF = idiopathic pulmonary fibrosis; REM = rapid eye movement.*

Mermigkis C et al. Chest 2017

Contents

- Sleep characteristics in ILD
- Prevalence
- Pathophysiological relationship between OSA and ILDs
- Clinical presentation and PSG characteristics
- Clinical outcomes
- Screening and diagnosis
- Treatment

Clinical presentation

No typical symptoms

- Daytime somnolence (~20%)
- Witness apnea (13-29%)
- Snoring (38-48%)

Frequent complaints

- Daytime fatigue (43-75%)
- Insomnia (52-67%)
- Nocturnal cough (48-56%)

Bouloukaki I et al. Breath 2022

PSG characteristics

Frequent hypopnea > apnea

Mermigkis C et al. Chest 2017
Bouloukaki I et al. Breath 2022

Contents

- Sleep characteristics in ILD
- Prevalence
- Pathophysiological relationship between OSA and ILDs
- Clinical presentation and PSG characteristics
- Clinical outcomes
- Screening and diagnosis
- Treatment

Clinical outcomes

OSA and IPF overlap

→ poor prognosis

1) Poor quality of life
2) Increased morbidity of ischemic heart disease
3) Poor survival ?

Quality of life in idiopathic pulmonary fibrosis: The impact of sleep disordered breathing

Marcello Bosi[a], Giulia Milioli[b,*], Liborio Parrino[b], Francesco Fanfulla[c], Sara Tomassetti[a], Andrea Melpignano[b], Irene Trippi[b], Anna Elisabetta Vaudano[b], Claudia Ravaglia[a], Susanna Mascetti[a], Venerino Poletti[a,d]

[a] *Department of Diseases of the Thorax, GB Morgagni Hospital, Asl Romagna, Forlì, Italy*
[b] *Sleep Disorders Center, Department of Medicine and Surgery, University of Parma, Italy*
[c] *Sleep Medicine Unit Istituti Clinici Scientifici Maugeri, IRCCS, Scientific Institute of Pavia, Italy*
[d] *Department of Respiratory Diseases & Allerg, Aarhus University Hospital, Aarhus, Denmark*

Prospectively enrolled IPF patients (n=34) who received a full-night PSG

	No SDB	OSA without nocturnal hypoxemia	OSA with nocturnal hypoxemia	P-value
ESS (median)	2.0	5.0	8.0	ns
PSQI (median)	4.0	5.0	8.5	ns
SGRQ (median)	35.4	49.5	64.0	0.04
ESS >10 (%)	0.0	0.0	37.5	0.02
PSQI ≥ 5 (%)	44.4	29.4	62.5	ns
SGRQ>95percentile (%)	22.2	58.8	62.5	ns

Bosi M et al. Res Med 2019

Obstructive sleep apnoea and related comorbidities in incident idiopathic pulmonary fibrosis

Thomas Gille[1,2], Morgane Didier[3], Marouane Boubaya[4], Loris Moya[5], Angela Sutton[6,7], Zohra Carton[3], Fanny Baran-Marszak[8,9], Danielle Sadoun-Danino[3], Dominique Israël-Biet[10,11], Vincent Cottin [12,13], Frederic Gagnadoux[14,15], Bruno Crestani[16,17], Marie-Pia d'Ortho[17,18], Pierre-Yves Brillet[2,5], Dominique Valeyre[2,3], Hilario Nunes[2,3], Carole Planès[1,2] and collaborators[19]

Newly diagnosed IPF patients (n=45)

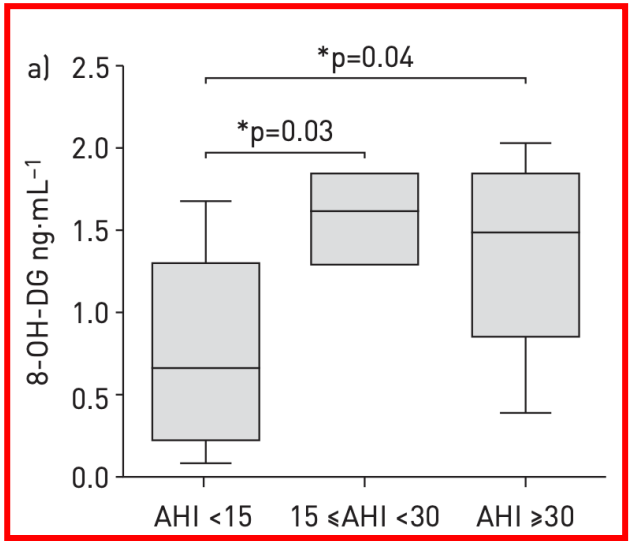
Gille T et al. Eur Respir J 2017

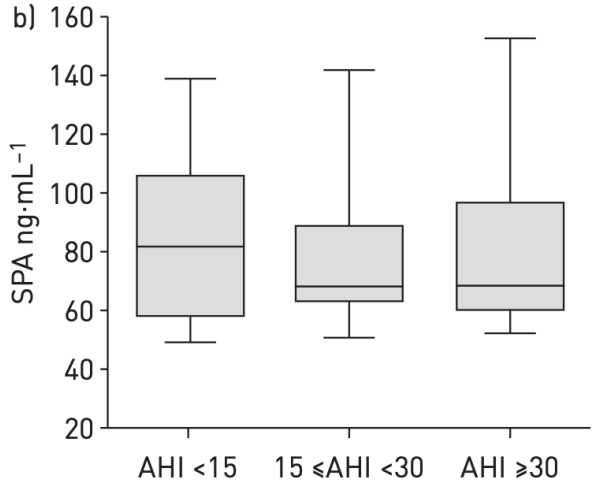
Characteristic	No OSA or mild OSA[#]	Moderate OSA[¶]	Severe OSA[+]	p-value
Subjects	17	10	18	
GER	4 (23.5)	1 (10)	9 (50)	0.08
Cardiovascular disease[§]	7 (41.2)	4 (40)	18 (100)	<0.0001
Hypertension	6 (35.3)	3 (30)	10 (55.6)	0.37
Ischaemic heart disease	2 (11.8)	3 (30)	11 (61.1)	0.009
Stroke/transient ischaemic attack	0 (0)	0 (0)	3 (16.7)	0.23
Peripheral arteriosclerosis	0 (0)	0 (0)	3 (16.7)	0.22
Aortic aneurysm	0 (0)	0 (0)	1 (5.6)	1
Thromboembolic disease	1 (5.9)	2 (20)	1 (5.6)	0.43
Pulmonary hypertension	0 (0)	0 (0)	0 (0)	1
Diabetes mellitus	2 (11.8)	1 (10)	5 (27.8)	0.41
Hyperlipidaemia	5 (29.4)	3 (30)	9 (50)	0.42
Smoking status				0.06
Never a smoker	5 (29.4)	7 (70)	3 (16.7)	
Former smoker	8 (47.1)	3 (30)	12 (66.7)	
Current smoker	4 (23.5)	0 (0)	3 (16.7)	
Prednisone treatment	6 (35.3)	1 (10)	3 (16.7)	0.24

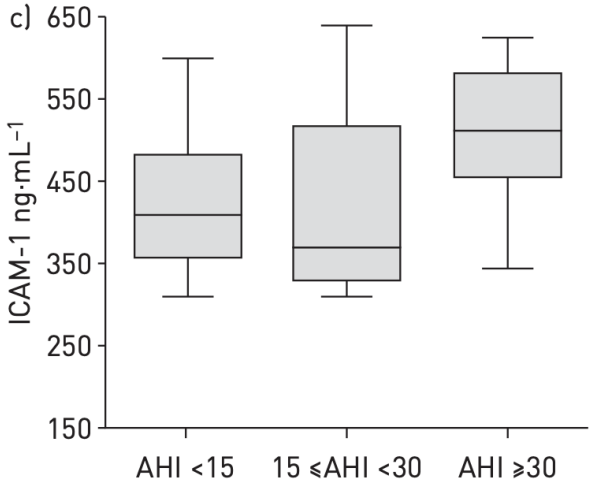
Data	No or mild OSA[#]	Moderate OSA[¶]	Severe OSA[+]	p-value
Subjects	12	8	14	
Fibrosis score	105.8±42.8	139.4±55.9	104.7±30.7	0.15
Coronary artery calcifications (grade >2)	4 (33.3)	2 (25)	12 (85.7)	0.005

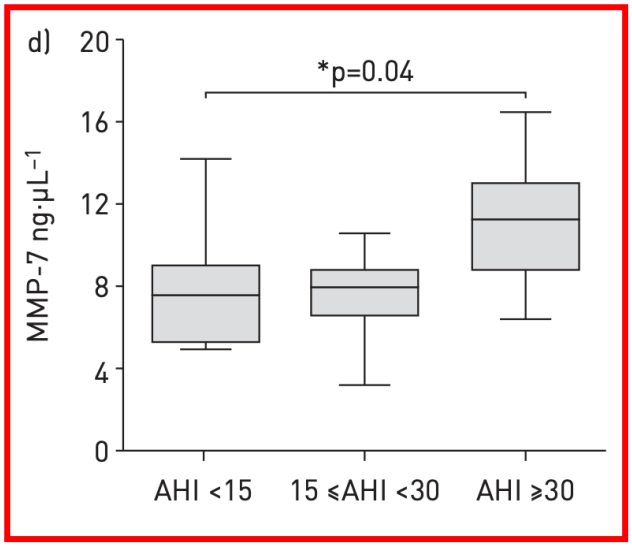
Gille T et al. Eur Respir J 2017

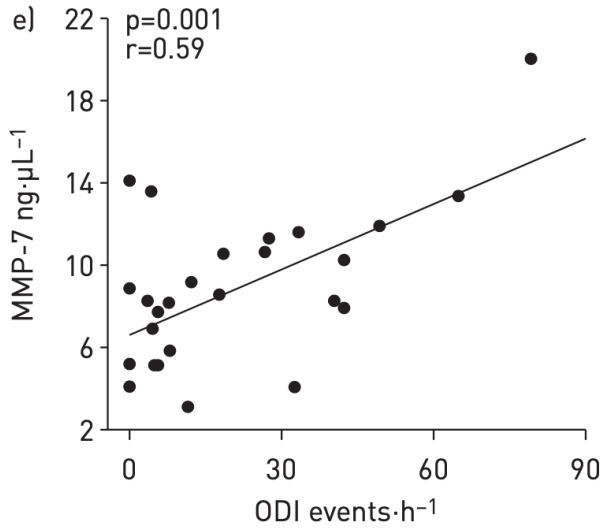
8-OH-DG: DNA oxidative damage











Gille T et al. Eur Respir J 2017

OSA and Prolonged Oxygen Desaturation During Sleep are Strong Predictors of Poor Outcome in IPF

Marcello Bosi[1] · Giulia Milioli[2] · Francesco Fanfulla[3] · Sara Tomassetti[1] · Jay H. Ryu[4] · Liborio Parrino[2] · Silvia Riccardi[2] · Andrea Melpignano[2] · Anna Elisabetta Vaudano[2] · Claudia Ravaglia[1] · Paola Tantalocco[1] · Andrea Rossi[4] · Venerino Poletti[1,2,3,4,5,6]

IPF patients (n=35)

→ 25 patients (71.5%) diagnosed with OSA

mild: 40%

moderate: 20%

severe: 11.5%

→ 8/25 patients (32%) presented sleep-related hypoxemia

Bosi M et al. Lung 2017

		No OSA	OSA without hypoxemia	OSA with hypoxemia	
	Whole group	Group A	Group B	Group C	ANOVA
RDI (ev/hr)	15.1 ± 15.9	2.5 ± 3^°	14.6 ± 9.8°	30.2 ± 22.5^	0.0004
RERA (ev/hr)	3.8 ± 4.3	1.1 ± 1.5^°	3.7 ± 2.1°	7.2 ± 7.1^	0.0080
AHI (ev/hr)	11.2 ± 13.2	1.4 ± 2.3^°	10.8 ± 10.5°	23 ± 16.8^	0.001
HI (ev/hr)	8.7 ± 9.9	0.98 ± 1.8^°	9.7 ± 9.8°	15.3 ± 10.7^	0.006
ODI (ev/hr)	10.6 ± 11.2	1.3 ± 2.2^°	11.2 ± 10.6°*	19.7 ± 11.3^*	0.001
SaO_{2w} (%)	93.7 ± 2.9	94.9 ± 2.8^	94.5 ± 2.4*	90.6 ± 1.9^*	0.001
SaO_2 (%)	92.4 ± 3.2	94.3 ± 2^	93.2 ± 2.5*	88.5 ± 2.5^*	<0.0001
T_{90} (%)	7.5 ± 12.2	1.4 ± 3.3^	3.7 ± 9.8*	22.3 ± 12.1^*	<0.0001

RDI respiratory disturbance index; *RERA* respiratory effort relate arousal; *AHI* apnea hypopnea index; *HI* hypopnea index; *ODI* oxygen desaturation index; SaO_{2w} average SpO_2 during wakefulness; *SaO2* average SpO_2 during sleep; T_{90} percentage of TST spent with SpO2 < 90%

^ $p < 0.01$ at post hoc analysis between Group A and C

* $p < 0.01$ at post hoc analysis between Group B and C

° $p < 0.01$ at post hoc analysis between Group A and B

Frequent hypopneas

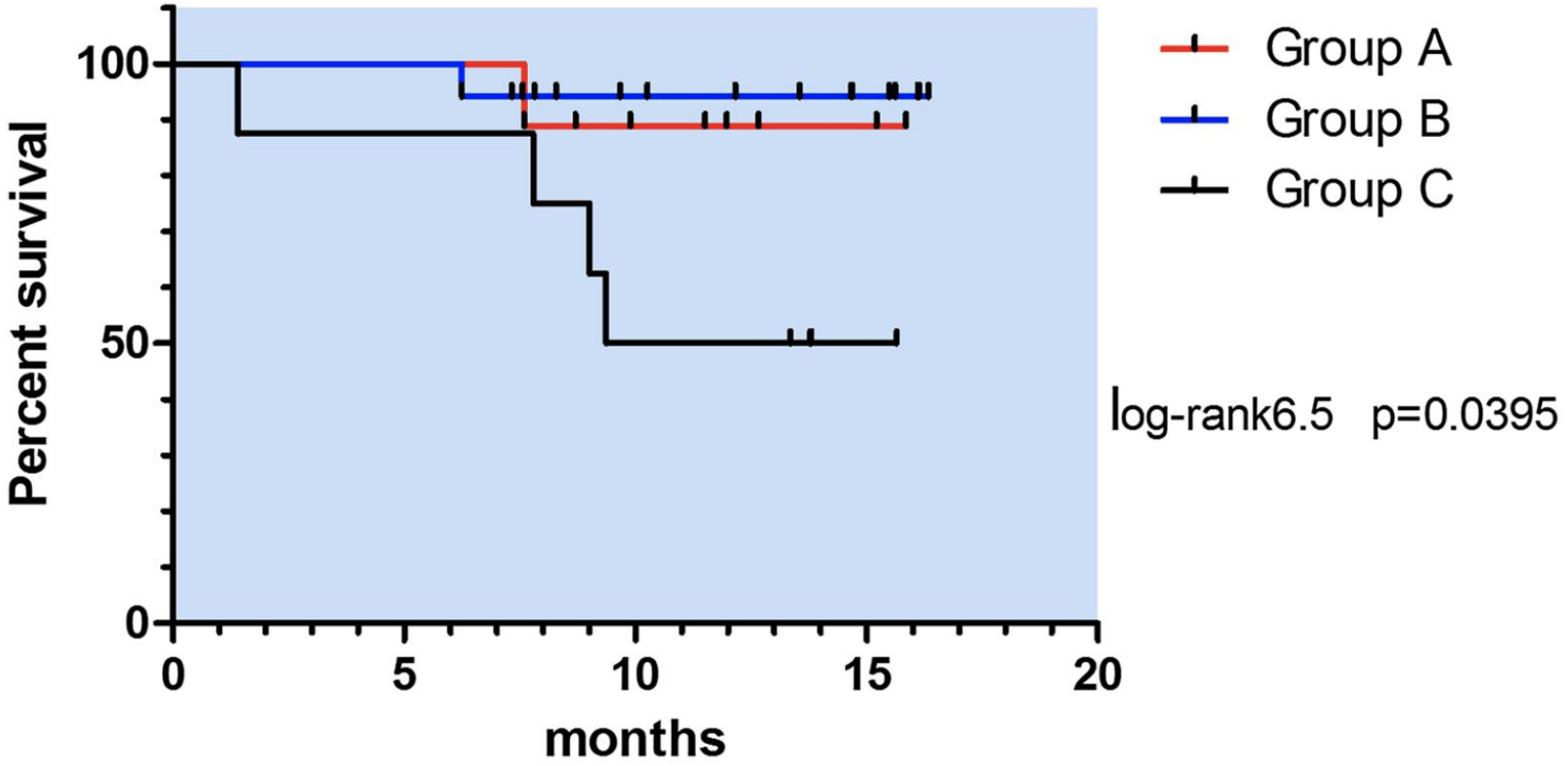
Bosi M et al. Lung 2017

		No OSA	OSA without hypoxemia	OSA with hypoxemia	
	Whole group	Group A	Group B	Group C	ANOVA
Age (yrs)	68.7 ± 9.2	66.2 ± 6.7	69.5 ± 9.4	69.7 ± 11.6	ns
BMI (Kg/m^2)	22.7 ± 3.7	21.3 ± 2.9	22.9 ± 4.1	23.8 ± 3.9	ns
Neck circumference (cm)	40.7 ± 2.8	40 ± 3.8	41.4 ± 2.3	40.1 ± 2.7	ns
FVC (%)	72.2 ± 19.6	73.8 ± 23.4	74.2 ± 16.6	66.1 ± 22.3	ns
FEV_1 (%)	79.2 ± 21.5	79.8 ± 26.9	82.9 ± 17	70.7 ± 23.9	ns
DLco (%)	45.6 ± 15.3	49 ± 15.2	48.7 ± 16.6	35.2 ± 7.1	ns
6MWD (m)	379.3 ± 121	398.9 ± 131.8	423.8 ± 102.9*	285 ± 93.7*	0.027
PaO_2 (mmHg)	75.1 ± 12	75.7 ± 12.4	80.9 ± 9.1*	65.3 ± 10.2*	0.008
$PaCO_2$ (mmHg)	38.7 ± 3.6	37.3 ± 1.95	39. ± 3.7	38.9 ± 4.4	ns
GAP points	4.2 ± 1.2	3.9 ± 1.2	4 ± 1.28	4.87 ± 0.64	ns

BMI body mass index; *FVC* forced vital capacity; *FEV1* forced expiratory volume in the first second; *DLco* diffusion lung capacity for carbon monoxide; *6MWD*: 6 Minutes Walking distance; PaO_2 arterial oxygen partial pressure; *$PaCO_2$* arterial carbon dioxide partial pressure

* $p < 0.01$ at post hoc analysis between Group B and C

Bosi M et al. Lung 2017

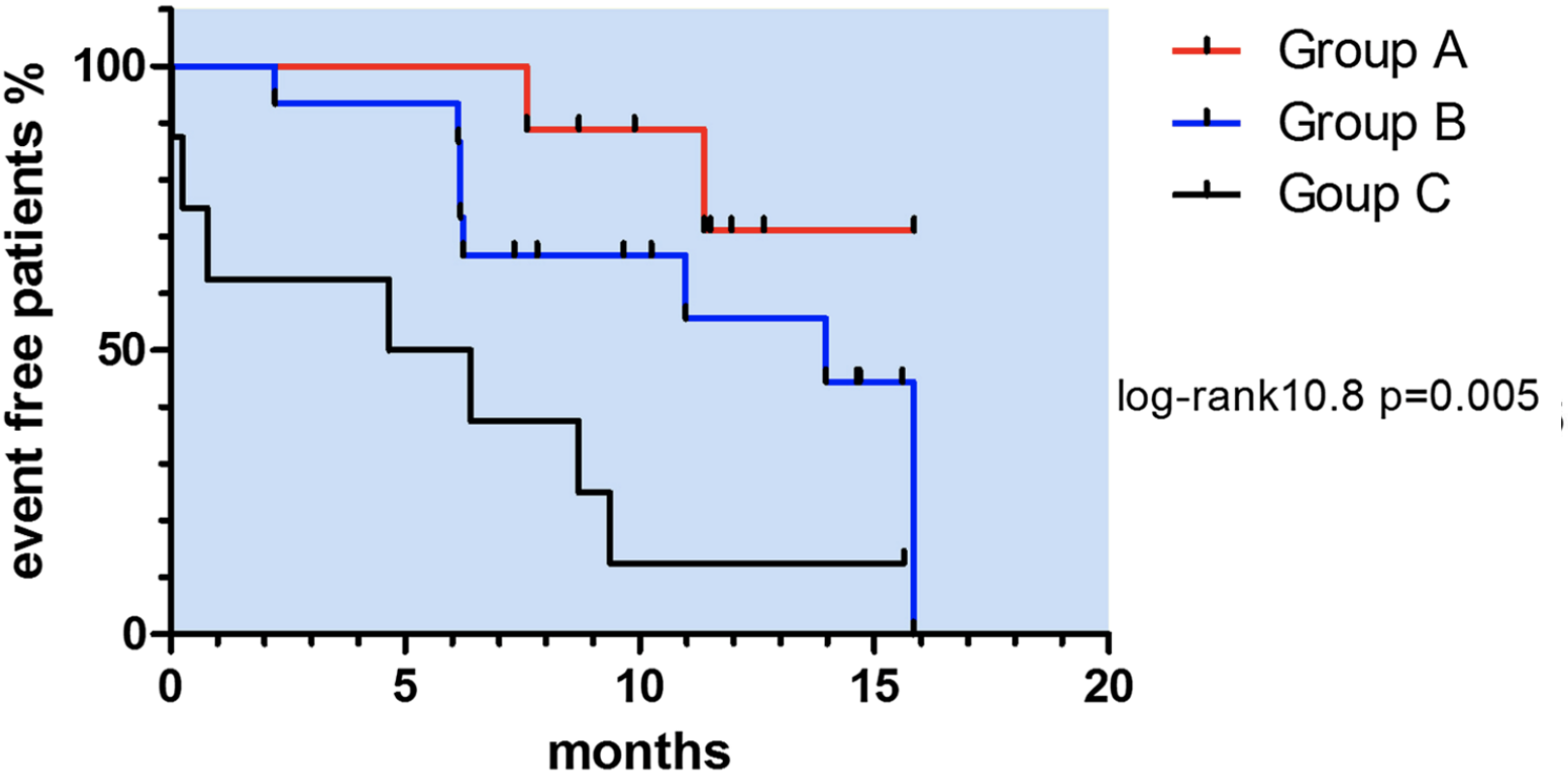


Cox proportional hazards multiple regression analysis for mortality

→ presence of **OSA associated with sleep-related hypoxemia** (HR 6.7; 95% CI 1.2–36.3; p=0.029).

*adjusted for FVC, DL_{CO}, 6MWD, GAP score, AHI, T_{90}

Bosi M et al. Lung 2017



Cox proportional hazards multiple regression analysis for disease progression

→ presence of **SDB**
(HR 3.1; 95% IC 1.4–6.3; p=0.003)

→ presence of **OSA associated with sleep-related hypoxemia**
(HR 9.0; 95% CI, 1.8–644.9; p=0.007)

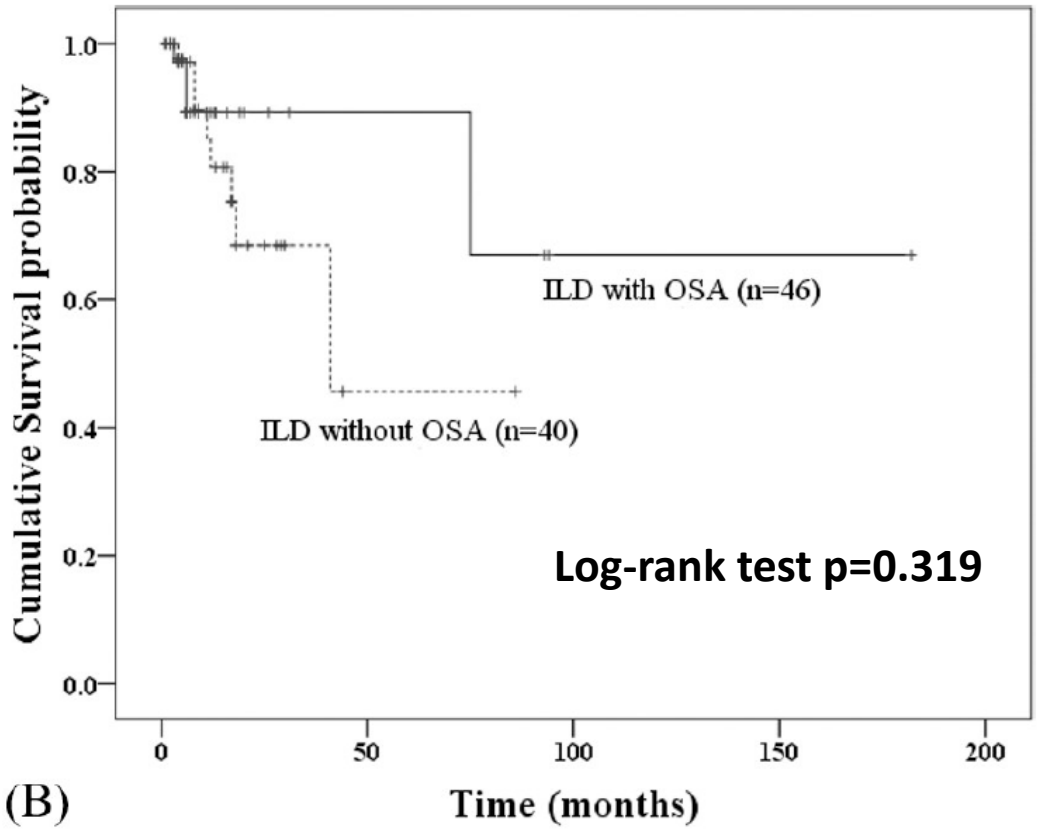
*adjusted for FVC, DL_{CO}, 6MWD, GAP score, AHI, T_{90}

Bosi M et al. Lung 2017

RESEARCH ARTICLE

Obstructive sleep apnea in patients with interstitial lung disease: Prevalence and predictive factors

Jae Ha Lee[1], Chan Sun Park[2], Jin Woo Song[3]*



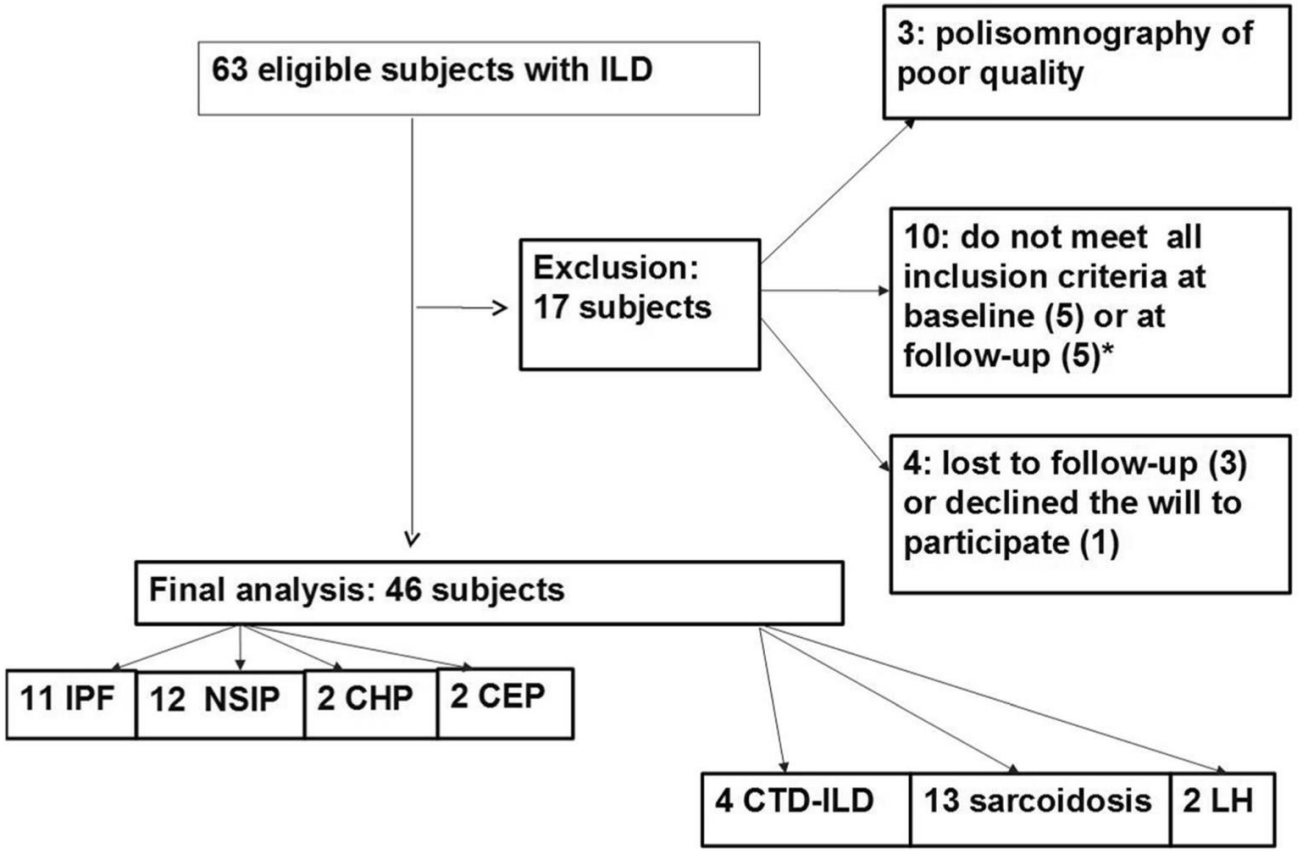
No significant difference

Lee JH et al. PLos One 2020

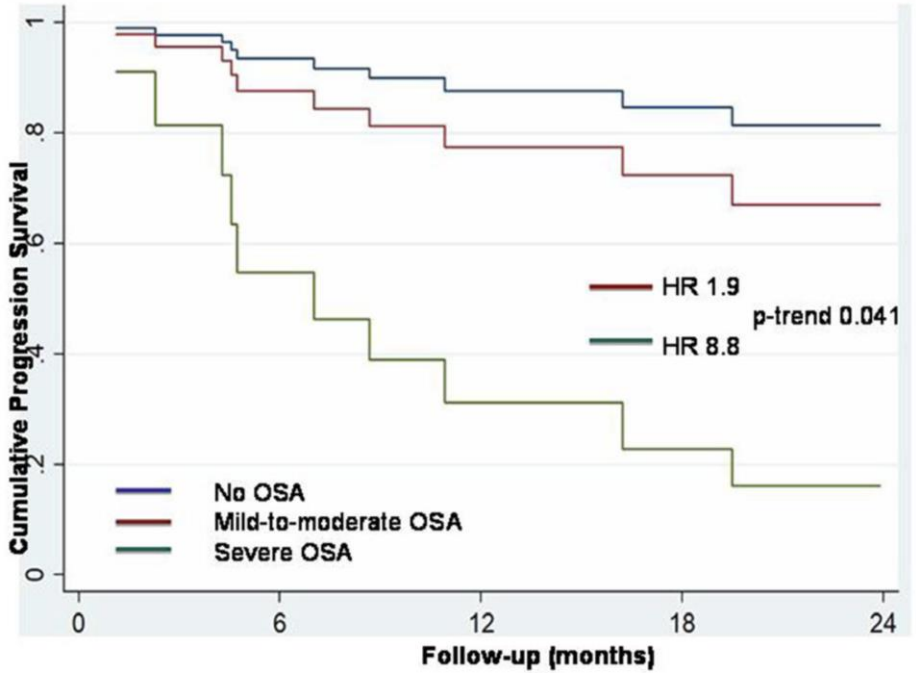
Prognostic Significance of Obstructive Sleep Apnea in a Population of Subjects with Interstitial Lung Diseases

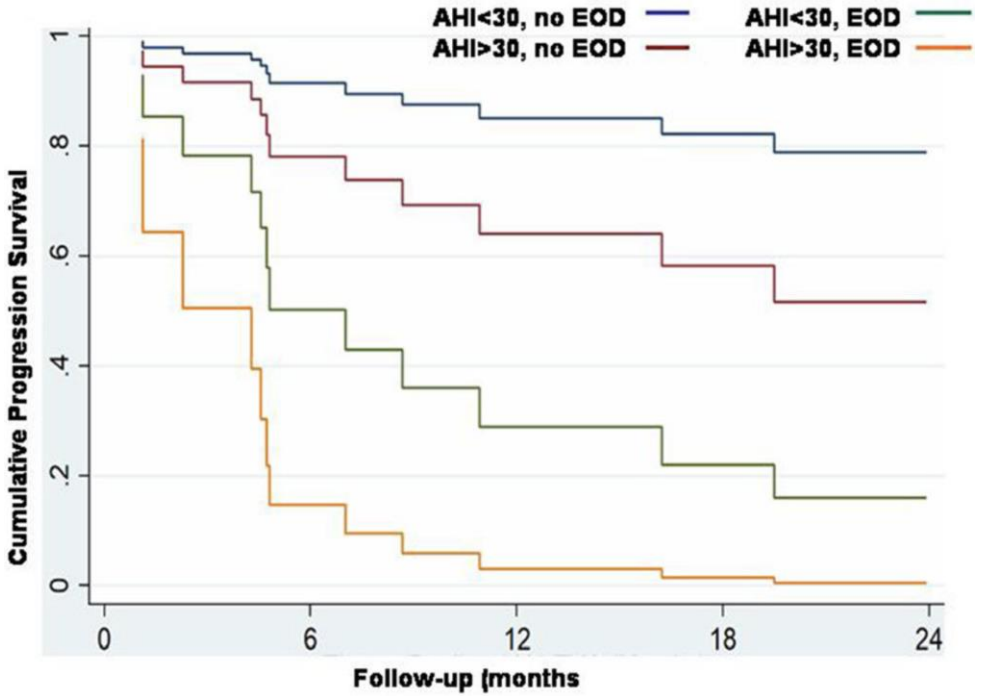
Debora Valecchi · Elena Bargagli · Maria Grazia Pieroni · Metella Rosa Refini · Piersante Sestini · Paola Rottoli · Andrea S. Melani

Prospective observational study
Type III polygraphy



Valecchi D et al. Pulm Ther 2023





Multivariate analysis for disease progression (death of FVC decline >10%)

→ presence of **exertional desaturation**
(HR 8.23; 95% CI 1.82–36.54; p=0.006)

→ presence of **severe OSA**
(HR 7.53; 1.83–30.64; p=0.005)

*Adjusted for composite physiologic index

Valecchi D et al. Pulm Ther 2023

Contents

- Sleep characteristics in ILD
- Prevalence
- Pathophysiological relationship between OSA and ILDs
- Clinical presentation and PSG characteristics
- Clinical outcomes
- Screening and diagnosis
- Treatment

Screening and diagnosis

No guidelines for screening for OSA in patients with ILD

ESS and other tools do not reliably predict the severity of sleep-related breathing disorders

STOP-BANG may be helpful for screening

PSG remains the gold standard diagnostic test for OSA

Contents

- Sleep characteristics in ILD
- Prevalence
- Pathophysiological relationship between OSA and ILDs
- Clinical presentation and PSG characteristics
- Clinical outcomes
- Screening and diagnosis
- Treatment

Treatment

CPAP

→ Treatment of choice in patients with OSA

→ Improved QOL and sleep-related outcomes

Obstructive sleep apnea should be treated in patients with idiopathic pulmonary fibrosis

Charalampos Mermigkis · Izolde Bouloukaki · Katerina Antoniou · Georgios Papadogiannis · Ioannis Giannarakis · Georgios Varouchakis · Nikolaos Siafakas · Sophia E. Schiza

Good compliance
→ Improved sleepiness and QoL

Table 2 Values of instruments used to assess quality of life and sleep at CPAP initiation and at the 1-year time point in the good and poor CPAP compliance group

	Good CPAP compliance group (n=37)			Poor CPAP compliance group (n=18)		
	CPAP initiation	After 1 year with CPAP	p	CPAP initiation	After 1 year with CPAP	p
ESS	9.2±5.6	5.8±3.8	0.04	7.1±3.2	6.2±5.5	0.45
BDI	12.1±5.1	7.7±4.2	0.01	11.8±5.8	12.2±4.2	0.81
PSQI	10.9±4.5	5.8±4.1	0.002	10.6±4.3	7.6±4.8	0.05
FOSQ	13.2±3.3	17.1±1.7	0.0002	13.5±3.2	12.7±3.6	0.22
FSS	40.9±11.1	27.9±8.6	0.0007	51.5±10.1	41.4±15.8	0.02
SF-36 physical component	60.8±12.4	76.4±11.6	0.008	53.7±18.3	63.8±18.1	0.08
Physical functioning (PF)	62.1±22.4	75.9±11.7	0.02	51.1±29.3	47.7±21.7	0.69
Role physical (RP)	65.2±28.3	80.7±18.6	0.03	50.2±27.3	52.8±21.6	0.63
Bodily pain (BP)	64.4±27	79.7±18.6	0.04	52.4±31.3	69.2±27.8	0.04
General health (GH)	53.5±16.2	68.1±13.4	0.009	48.5±19.2	53.9±17.2	0.09
SF-36 mental health component	65.3±17.1	79.5±10.3	0.007	61.2±20.4	66.5±16.4	0.36
Vitality (VT)	61.5±15.7	72.1±13.7	0.04	52.5±19.4	63.1±16.3	0.04
Social functioning (SF)	77.2±16.8	90.6±11.6	0.01	74.4±21.6	76.1±17.8	0.78
Role emotional (RE)	63.6±23.9	80.7±13.5	0.02	56.5±29.1	66.8±22.9	0.29
Mental health (MH)	59.2±22.7	74.7±14.7	0.03	60.3±20.1	61.6±18.7	0.97

ESS Epworth Sleepiness Scale, *BDI* Beck Depression Inventory, *PSQI* Pittsburgh Sleep Quality Index, *FOSQ* Functional Outcomes of Sleep Questionnaire, *SF-36* Short-Form 36 Health Survey, *FSS* Fatigue Severity Scale

CPAP Adherence, Mortality, and Progression-Free Survival in Interstitial Lung Disease and OSA

Ayodeji Adegunsoye, MD, FCCP; Julie M. Neborak, MD; Daisy Zhu, MD; Benjamin Cantrill, DO; Nicole Garcia, BS; Justin M. Oldham, MD; Imre Noth, MD, FCCP; Rekha Vij, MD; Tomasz J. Kuzniar, MD, PhD; Shashi K. Bellam, MD, FCCP; Mary E. Strek, MD, FCCP; and Babak Mokhlesi, MD, FCCP

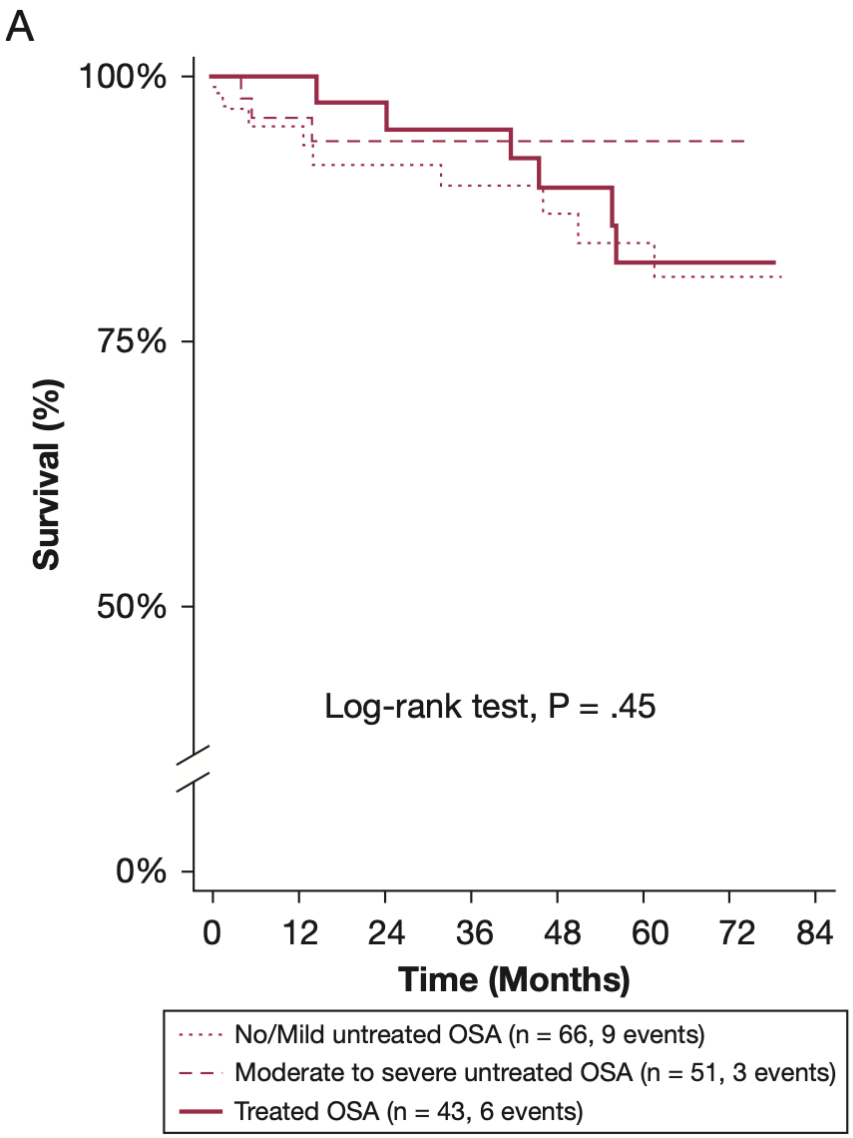
10-year retrospective observational multicenter cohort study

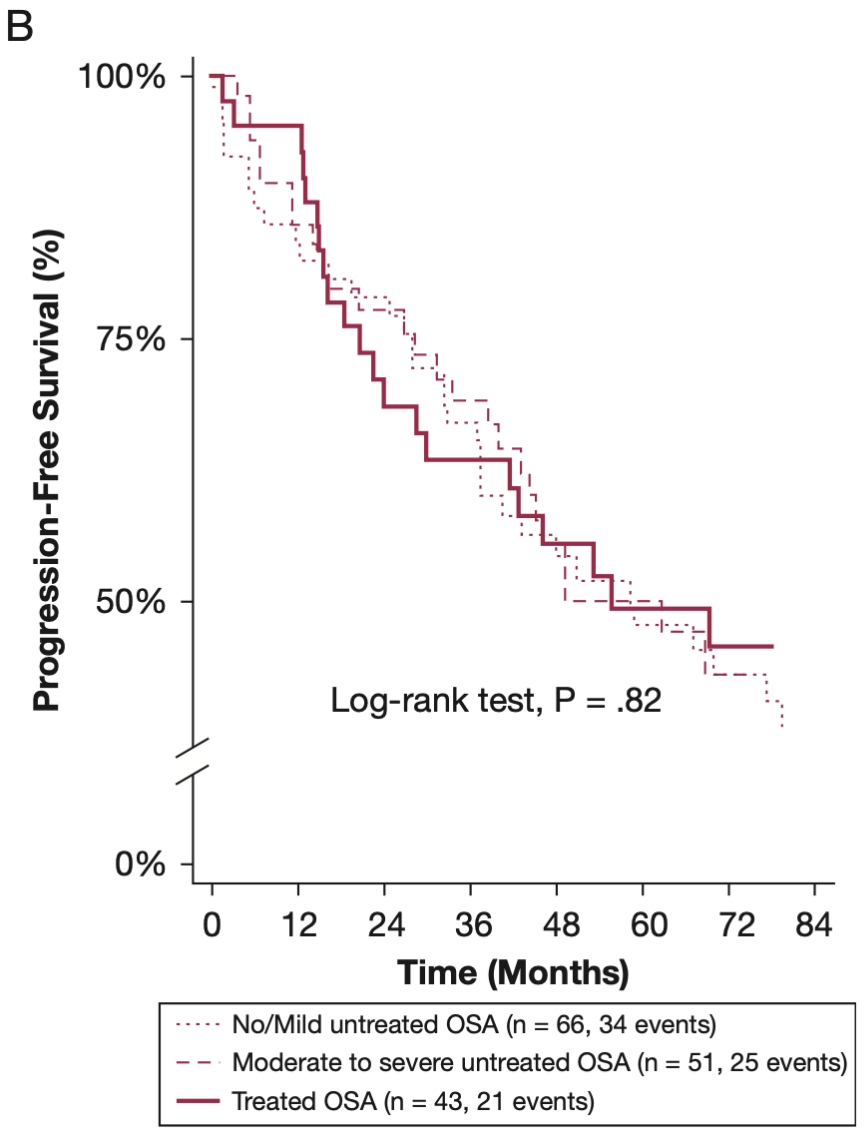
Patients with ILD & OSA (n=160)
- No/mild OSA (n=66)
- Mod/severe untreated OSA (n=51)
- Treated OSA (n=43)

*treated OSA: CPAP use ≥4h/night on ≥70% of days during the first 30 days

Adegunsoye A et al. Chest 2020

CPAP use → no survival benefit

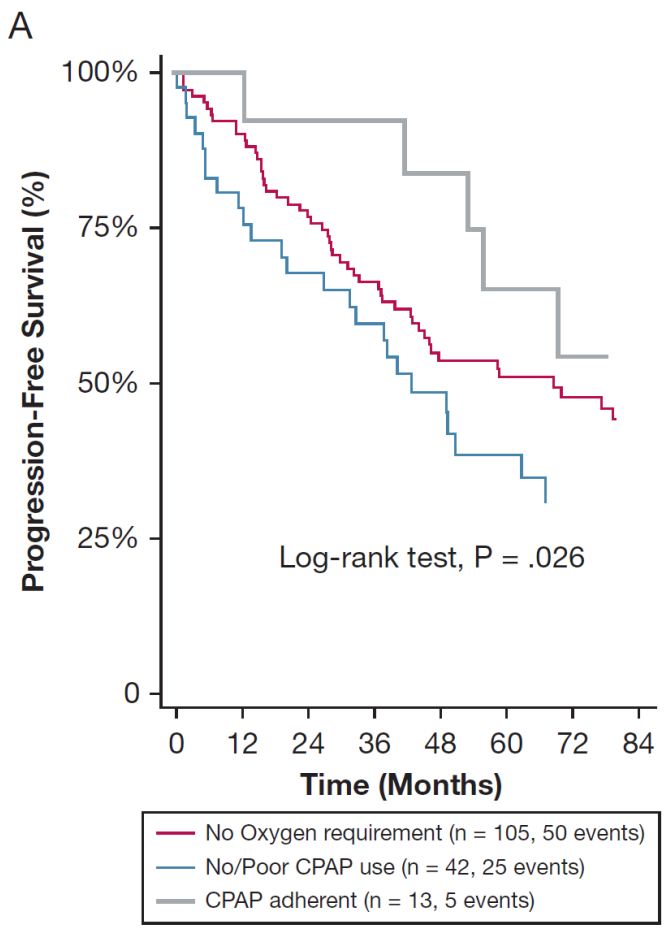


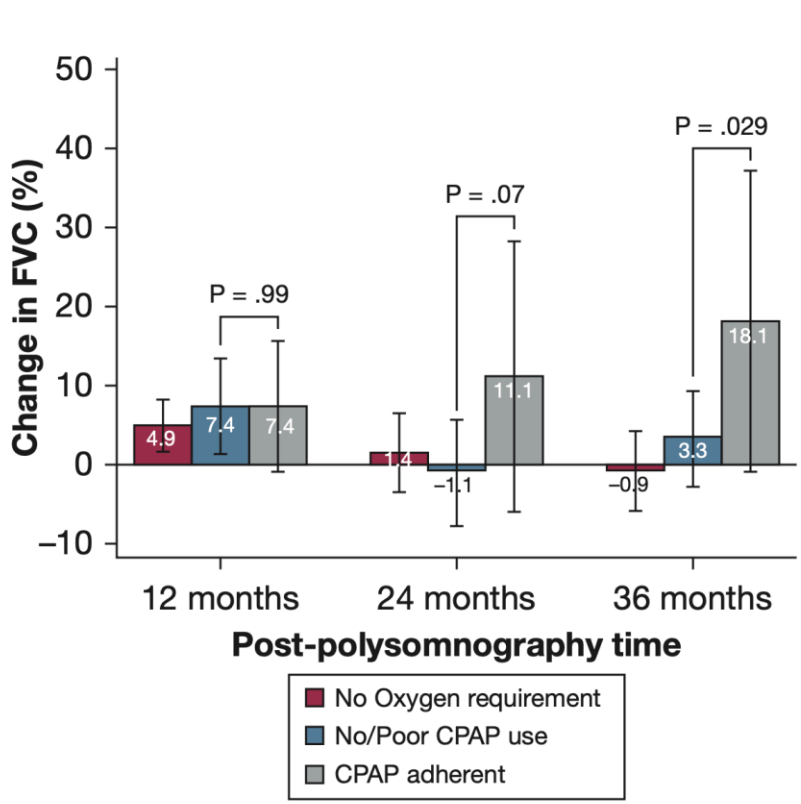


Adegunsoye A et al. Chest 2020

Characteristics	All Patients (N = 160)	No/Mild Untreated OSA (n = 66)	Moderate to Severe Untreated OSA (n = 51)	Treated OSA (n = 43)	*P* Value[a]
Oxygen supplementation					
No supplemental oxygen requirement	105 (65.6)	46 (69.7)	29 (56.9)	30 (69.8)	.28
Require supplemental oxygen	55 (34.4)	20 (30.3)	22 (43.1)	13 (30.2)	…

Among those with supplemental oxygen requirement





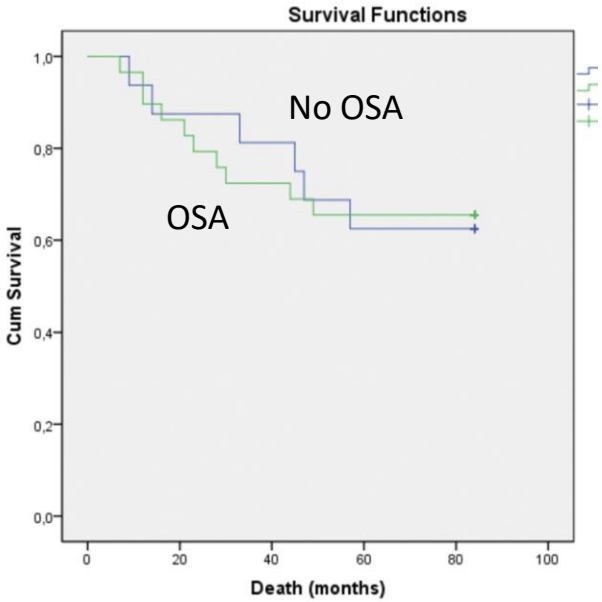
Adegunsoye A et al. Chest 2020

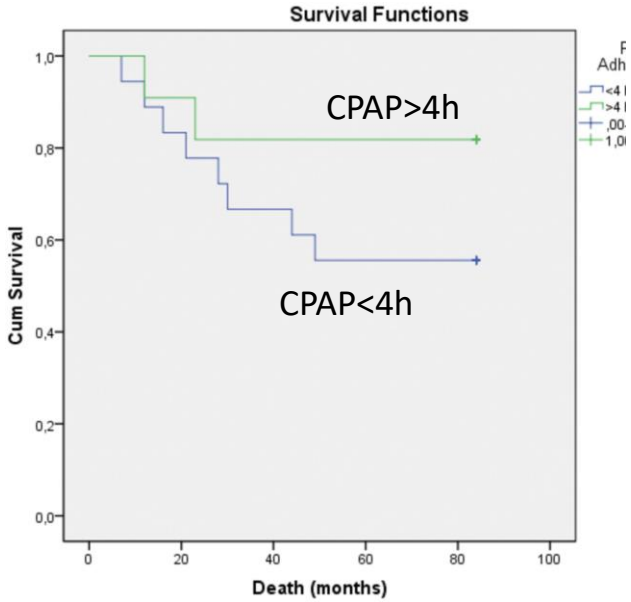
Patients with idiopathic pulmonary fibrosis with and without obstructive sleep apnea: differences in clinical characteristics, clinical outcomes, and the effect of PAP treatment

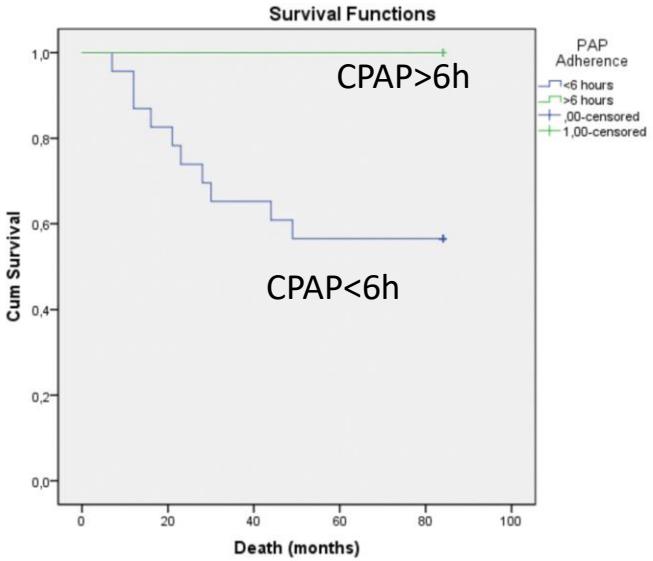
George Papadogiannis, MD[1,*]; Izolde Bouloukaki, MD, PhD[1,*]; Charalampos Mermigkis, MD, PhD[1]; Stylianos Michelakis, MD[1]; Christina Ermidou, MD[1]; Eleni Mauroudi, RN[1]; Violeta Moniaki, RN[1]; Nikolaos Tzanakis, MD, PhD[1]; Katerina M. Antoniou, MD, PhD[2,**]; Sophia E. Schiza, MD, PhD[1,**]

*[1]Sleep Disorders Center, Department of Respiratory Medicine, University of Crete, Heraklion, Greece; [2]Department of Respiratory Medicine, Interstitial Lung Disease Unit, Pneumonology Molecular & Cellular Lab, Faculty of Medicine, University of Crete, Heraklion, Greece; *Contributed equally as co-first authors; **Contributed equally as co-last authors*

Newly diagnosed IPF patients (n=45), followed up for 7 years
with OSA (n=29) vs. without OSA (n=16)







Papadogiannis G et al. J Clin Sleep Med 2021

Summary

Limitations of studies to date

- Small number of patients included
- No large prospective data
- Not all studies employed level-1 sleep study

> Hypopnea rule
> EEG for arousal determination and nasal pressure transducer device in addition to a thermistor for airflow measurement

- Lack of concrete data on the treatment benefit

Summary

1. OSA is prevalent in patients with ILD
2. Bidirectional relationship exists between OSA and ILD
3. Fatigue is common rather than typical symptoms suggestive of OSA
4. OSA is associated with worse clinical outcomes
   - poor quality of life
   - increased morbidity of IHD
   - survival (?): poor survival in case of nocturnal desaturation
5. CPAP is the treatment of choice, but its clinical benefit should be further investigated