



Patient with $FVC > 90\%$ predicted

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CASE OVERVIEW

A 63-year-old, male patient with progressive exertional dyspnoea lasting for 2 years and dry cough showed a mild reduction of DL_{CO} at initial lung function testing. An initial HRCT revealed a possible UIP pattern including reticular abnormalities and traction bronchiectasis. Functional follow-up testing showed preserved FVC despite progressive reduction in DL_{CO} .

This is a case that shows that preserved lung volumes do not exclude IPF even in the absence of emphysema. Also, DL_{CO} deterioration seems to correlate better with progression of fibrosis on HRCT.

MEDICAL HISTORY AND TESTS

Basic data

- Male, 63 years old
- Symptoms: progressive dyspnoea on exertion during the last 2 years, dry cough
- Smoking status: never smoker
- Occupation: banker (office worker), no exposure allergens, irritants
- No comorbidities

MEDICAL HISTORY AND TESTS

Physical examination

Lung auscultation: Velcro-like crackles with basal predominance

- No digital clubbing
- No leg oedema
- No arthralgia
- SpO₂: 97% (on ambient air)
- Heart rate: 80 bpm

Cardiology evaluation

- RVSP: 30 mmHg

LABORATORY

- Normal CBC, biochemistry
- ANA: 1/160
- RF, anti-CCP, ENA panel: negative

LUNG FUNCTION

Initial tests

Parameter	Value
FVC	97% predicted
FEV ₁ /FVC	89%
TLC	80% predicted
DL _{CO}	71% predicted

Conclusion:

- Mild reduction of DL_{CO}
- Borderline reduction in TLC

IMAGING

Initial HRCT

- Irregular reticular pattern with subpleural distribution and lower zone predominance
- Traction bronchiectasis/bronchiolectasis
- No inconsistent features with a UIP pattern
- Conclusion: Possible UIP pattern

Slice thickness: 1.0 mm

QUESTION 1

Which of the following is true?

- A. Treatment with nintedanib could be indicated
- B. Treatment with pirfenidone could be indicated
- C. No treatment is indicated because of relatively preserved lung volumes (FVC: 97% predicted, TLC: 80% predicted)
- D. No treatment is indicated because there is no definite honeycombing on HRCT and because there is no biopsy confirmed diagnosis

ANSWER 1

Author's solution: Correct answer: A, B

A post hoc subgroup analysis of the INPULSIS® clinical trial showed same effect of nintedanib on annual rate of decline in FVC, time to first acute exacerbation and change in SGRQ total score over 52 weeks in patients with preserved/marginally impaired lung function (FVC >90% predicted) vs patients with more impaired lung function (FVC < 90% predicted) and also in patients without honeycombing or biopsy vs patients with honeycombing and/or biopsy. The annual rate of decline in FVC in the placebo groups was similar in patients with marginally impaired lung function and in patients with more advanced lung function impairment. These findings suggest that 1. patients with marginally impaired FVC (>90% predicted) benefit from treatment with nintedanib and 2. presence or absence of honeycombing and/or biopsy did not have an effect on the treatment outcome.^{1,2} Pooled data from the ASCEND and CAPACITY clinical trials showed similar treatment effects of pirfenidone on rate of decline in FVC and 6MWD, in patients with baseline FVC ≥ 80% and GAP1 vs patients with baseline FVC < 80% or GAP2-3.³

Based on these findings, the official IPF treatment guideline update from 2015 included a conditional recommendation for the use of pirfenidone and nintedanib.⁴

1. Kolb M et al. *Am J Respir Crit Care Med* 191;2015:A1021.
2. Raghu G et al. *Am J Respir Crit Care Med* 191;2015:A1022.
3. Albera C et al. *Am J Respir Crit Care Med* 191;2015:A1018.
4. Raghu g et al. *Am J Respir Crit Care Med* 192;2015:e3–e19.

OUTPATIENT CLINIC

- The patient was unwilling to start therapy with anti-fibrotic agents.
- He reported back to our centre after 22 months due to further worsening of his dyspnoea.
- New physical, laboratory and cardiology evaluation did not disclose any new findings.
- In the meanwhile, the patient was monitored by a private respiratory physician and was subjected to serial pulmonary function tests.

LUNG FUNCTION

Follow-up 13 months later

Date	FVC (% pred)	FEV ₁ /FVC (%)	TLC (% pred)	DL _{CO} (% pred)
Baseline	97	89	80	71
After 4 months	92	91	72	61
After 8 months	79	92	78	51
After 12 months	86	92	70	52
After 18 months	90	92	-	46

→ Progressive reduction in DL_{CO} is noted, with preserved FVC

QUESTION 2

What is considered a bad prognosticator in the outcome of IPF?

- A. A baseline $DL_{CO} < 35\%$
- B. A decrease in $DL_{CO} > 15\%$ in 6 months
- C. A decrease in $FVC > 5\%$ in 6 months
- D. All of the above
- E. None of the above

ANSWER 2

Author's solution: Correct answer: D

- DL_{CO} trends are strongly predictive of survival when dichotomised as a significant (more than 15% of baseline) decline or stability/improvement.¹
- A decline in percent-predicted FVC $\geq 10\%$ at 24 weeks is associated with a nearly five-fold increase in the risk of mortality over the subsequent year, whereas a decline of 5–10% is associated with a two-fold increase in the risk of 1-year mortality.²

1. Latsi PI, du Bois RM, Nicholson AG et al. *Am J Respir Crit Care Med* 2003;168:531-537.
2. Du Bois RM et al. *Am J Respir Crit Care Med* 2011;184(12):1382-1389.

IMAGING

HRCT



Initial HRCT
(upper row: level of bronchus intermedius, lower row: level of RB6)

Follow-up HRCT 13 months later
(upper row: level of bronchus intermedius, lower row: level of RB6)

QUESTION 3

The extent of fibrosis on the follow up HRCT is:

- A. Stable
- B. Increased
- C. Decreased

ANSWER 3

Author's solution: Correct answer: B

The observed irregular reticular pattern has increased in extent as well as in density. Also, new areas of traction bronchiectasis are noted.

EXPERT OPINION

It is indeed difficult for some patients (particularly in early stages when symptoms are mild and self-manageable) to accept the necessity of a chronic treatment.

However, IPF is a relentlessly progressive disease. There are encouraging data regarding the efficacy of both pirfenidone and nintedanib in IPF patients with preserved lung volumes (FVC >80% pred. at baseline and FVC >90% pred. at baseline, respectively).¹⁻³ This actually coincides with common sense. It is reasonable that early intervention preserves more functional lung parenchyma. In addition to this, data with nintedanib have shown to reduce the risk of an acute exacerbation occurring in a fibrotic lung.⁴

For further reading:

1. Kolb M et al. *Am J Respir Crit Care Med* 191;2015:A1021.
2. Raghu G et al. *Am J Respir Crit Care Med* 191;2015:A1022.
3. Albera C et al. *Am J Respir Crit Care Med* 191;2015:A1018.
4. Richeldi et al. *N Eng J Med* 370;2014.2071-82.

LEARNINGS FROM THE CASE

- 1) Preserved lung volumes do not exclude IPF even in the absence of emphysema.
- 2) Current data support the initiation of antifibrotic treatment in IPF patients with preserved lung volumes (FVC>80%).
- 3) Despite the preserved FVC, DL_{CO} deterioration seems to correlate better with progression of fibrosis on HRCT.^{1,2}

1. Wells AU et al. Am J Respir Crit Care Med. 1997;155:1367-1375.

2. Park KH et al. Eur J Cardiothorac Surg. 2007;31:1115-1119.

More patient cases can be found on www.inIPF.com