Recruitment

Patients were pre-screened from the ILD clinic according to eligibility criteria and history of desaturation on exercise on incremental walk testing.

Eligible patients (n=40) first performed an incremental CPET in a cycloergometer using the Customed Software. This test was performed on room air, but if patients desaturated during the test, oxygen was provided to maintain an oxygen saturation above 88%. Patients who did not desaturate below 90% at the end of the incremental test were excluded from the study. After screening, 18 patients were finally included in the study (fig 1).

Participant flow diagram

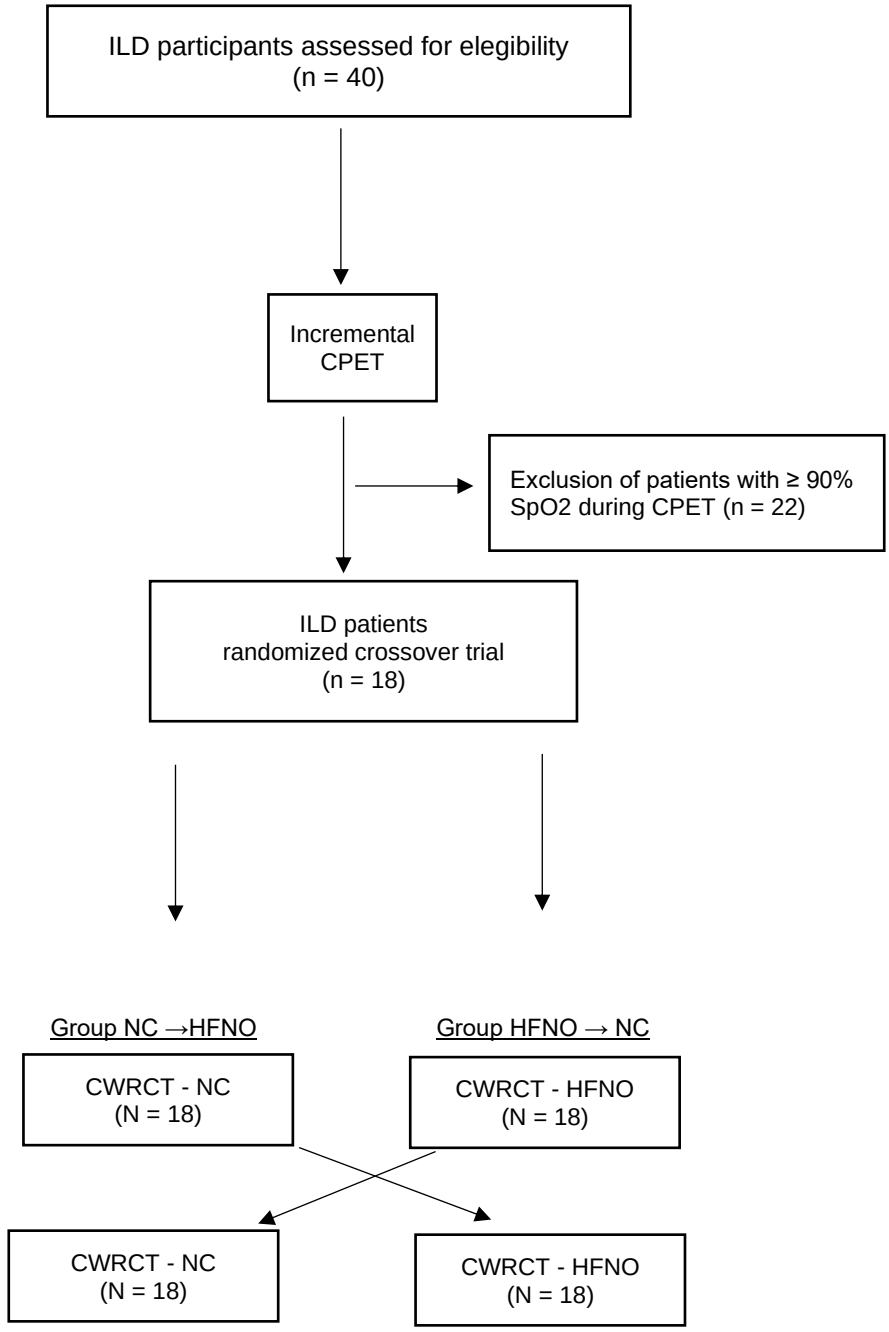

Figure 1. Participant flow diagram. ILD: interstitial lung disease; CPET: cardiopulmonary exercise test; SpO2: oxygen saturation; CWRCT: constant work rate cycle test; NC: nasal cannula; HFNO: high flow nasal oxygen

Results

40 patients with FILD were screened for eligibility. After screening, 18 FILD patients were randomized to perform the first test receiving supplemental oxygen first via HFNO or NC. Then, patients were crossover to perform the second test receiving supplemental oxygen via the other method. The 18 participants completed the study. Baseline characteristics are shown in Table 1 and their types of ILD are shown in table 2. There were no significant differences in any of the data between NC→HFNO and HFNO → NC groups. Fifteen of these patients (83%) showed an improvement more than 2 minutes in the endurance time using HFNO, who therefore were considered responders. On the other hand 9 patients (50%) were considered responders using NC.

Primary outcome

We found a statistically significant difference ($p<0.05$) in favour of HFNO in: endurance time (tLIM).

Secondary Outcomes

We found a statistically significant change ($p<0.05$) in favour of HFNO in:end oxygen saturation, nadir oxygen saturation, end dispnea (Borg scale), isotime heart rate (HR), isotime oxygen saturation and isotime dispnea (Table 3). Isotime values for all variables were defined at the end of the CWRCT performed without supplemental oxygen.

Table 1. Baseline characteristics of included patients.

	All Patients	NC→HFNO (N=11)	HFNO → NC (N=7)
Age (years)	68.5 ± 9.8	69.9 ± 8.2	66.4 ± 12.4
Sex, M/F	11/7	8/3	3/4
BMI (Kg/m2)	30.6 ± 5.5	31.2 ± 6.7	29.8 ± 3.4
Smoking status Never/Ex/Current	4/ 12/2	2/7/2	2/5/0
Pack-years	15.4 ± 15.4	19.7 ± 16.4	8.7 ± 11.9
FVC (L)	2.6 ± 0.9	2.8 ± 1.0	2.2 ± 0.6
FVC (%)	76.0 ± 21.8	80.2 ± 22.9	69.3 ± 19.5
DLCO (mmol/min/kpa)	3.3 ± 0.7	2.7 ± 0.3	3.2 ± 0.6
DLCO (%)	44.1 ± 11	35.0 ± 4.2	44.0 ± 12.3
mMRC	2.4 ± 0.8	2.0 ± 0.7	1.8 ± 0.5
Oxygen therapy (Yes/No)	9/9	5/6	4/3
Flow (L/min)	1.7 ± 0.6	2.4 ± 0.8	2.0 ± 0.0
Pulmonary hypertension RVSP >35 mmHg (Yes/No)	7 / 11	5/7	2/4
Antifibrotics (Yes/No)	4/ 14	1/10	3/4
Baseline CWRCT Endurance time (min)	3.5 ± 1.5	3.9 ± 1.8	3.9 ± 1.2
Nadir SpO2 (%)	82.5 ± 5.5	82.0 ± 4.1	81.4 ± 7.4
Max HR (bpm)	128.5 ± 19.2	123.0 ± 22.3	127.2 ± 14.2
Dyspnoea (Borg)	5.0 ± 2.3	5.5 ± 2.4	6.1 ± 2.2
Leg fatigue (Borg)	4.0 ± 2.0	4.7 ± 2.2	4.1 ± 1.8

NC: nasal cannula, HFNO: high flow nasal oxygen. Data are presented as number or mean ± standard deviation (SD). P-value from Student's t-test. Pulmonary hypertension was assessed by echocardiography (RVSP: right ventricular systolic pressure > 35 mmHg). BMI: body mass index, FVC: forced vital capacity, DLco: diffusion capacity for carbon monoxide, mMRC: the modified Medical Research Council dyspnea scale, CWRCT: constant work-rate cycle test, HR: heart rate, bpm: beats per minute.

Table 2. Types of ILD of the included patients.

Type of ILD	N = 18
uIIP	7
fHP	4
IPF	2
NSIP	1
CTD-ILD	1
Asbestosis	1
Sarcoidosis	1
Histiocytosis X	1

uIIP: idiopathic interstitial pneumonia; fHP: fibrotic hypersensitivity pneumonitis; IPF: idiopathic pulmonary fibrosis; ; NSIP: non-specific interstitial pneumonia; CTD-ILD: connective tissue disease-associated interstitial lung disease

Table 3. Primary and secondary endpoints (NC and HFNO)

	NC	HFNO	Difference (95% CI)	p - value
Responders	9 (50%)	15 (83%)		
Endurance time (min)	7.5 (4.5)	10.8 (6.9)	-3.3 (-4.8 – -1.7)	<0.001
End SPO2 (%)	88.7 (2.5)	92.7 (3.6)	-4 (-5.4 – -2.5)	<0.001
HR (bpm)	131.6 (19.4)	125.1 (23.8)	6.4 (-5.7 - 18.6)	0.282
Nadir SPO2	84.9 (3.1)	88.4 (2.8)	-3.5 (-4.5 – -2.4)	<0.001
Max HR (bpm)	141.2 (20.1)	133.5 (17.8)	7.7 (-1.7 - 17.2)	0.104
Dyspnoea (Borg)	5.2 (2.3)	4.2 (1.5)	1.0 (0.3 – 1.7)	0.007
Leg fatigue (Borg)	4.8 (2.1)	4.9 (2.5)	-0.1 (-0.8 – 0.5)	0.677
Patient's comfort	7.2 (1.7)	7.9 (1.3)	-0.7 (-1.7 - 0.2)	0.100
Isotime SPO2 (%)	89.2 (3.6)	93.2 (4.4)	-3.9 (-6.0 - -1.8)	<0.001
Isotime HR (bpm)	124.1 (17.2)	112.5 (23.8)	11.6 (3.7 – 19.3)	0.006
Isotime Dyspnoea (Borg)	3.4 (1.5)	2.6 (1.4)	0.8 (0.1 – 1.3)	0.015
Isotime Leg fatigue (Borg)	3.3 (1.6)	3.5 (2.2)	-0.2 (-0.9 – 0.5)	0.596

Data are mean (SD). SpO2: oxygen saturation, HR: heart rate, bpm: beats per minute

No adverse events were reported