our knowledge, ILD has never previously been related to heterozygous *SFTPB* mutation in either adults or children.

The patient's clinical situation was characterised by a normal pulmonary pressure and a transient need for oxygen supplementation; only low doses of oral prednisone were required. Presently, it is not possible to predict the patient's clinical course, as no other similar cases have been reported. Lung transplantation currently represents the only treatment option for this disease, but it is hoped that new treatments will be developed that are based on a better understanding of the disease.

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Statement of Interest: None declared.

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DOI: 10.1183/09031936.00155310

Ambulatory oxygen in interstitial lung disease

To the Editors:

Interstitial lung diseases (ILDs) are often associated with significant oxygen desaturation on exercise, resulting in exercise limitation, exertional dyspnoea and reduced quality of life. However, surprisingly few data are available on ambulatory oxygen in ILD. The 6-min walk test (6MWT), a self-paced test performed according to standardised protocols, has been shown to be highly reproducible in ILD patients [1], and is felt to be more sensitive than a cycle ergometer test in assessing oxygen requirements [2].

We present a retrospective assessment of the effects of ambulatory oxygen on 6MWT performance in a group of patients with fibrotic ILD seen at the Interstitial Lung Disease Unit, Royal Brompton Hospital, London, UK. The 6MWT was performed following a standardised protocol [3, 4]; patients were asked to perform the 6MWT at their habitual walking pace and were allowed to stop if they experienced unacceptable symptoms of dyspnoea and/or fatigue; standardised encouragement to restart the test was given at regular intervals.

A review of the clinical records of ILD patients seen at the Royal Brompton Hospital, from November 2007 to January 2010, identified 52 ILD patients with a fall in arterial oxygen saturation (S_{a,O_2}) $\leqslant$88% at the end of a baseline 6MWT, who had consented to a second test on ambulatory oxygen during the same session, as part of their routine clinical assessment. All 6MWTs were performed on the same measured corridor and were supervised by the same experienced oxygen technician (A. Montgomery), with a minimum rest period of 20 min between tests. Measurements included 6-min walk distance (6MWD), S_{a,O_2}, heart rate, and modified Borg dyspnoea score (range 1–10) assessed immediately before and after each 6MWT [5]. Recovery times to baseline S_{a,O_2}, heart rate, and Borg score were also measured at the end of each test. In 32 patients, the baseline 6MWT was performed on room air, whereas the habitual oxygen flow rate at rest was used for the others, and an increased flow rate was used for the second test. Ambulatory oxygen was provided by using the same Sabre cylinder (Aldershot, UK), weighing 6.5 lbs (2.9 kg). To mirror the patient's daily needs, the oxygen cylinder was carried by the patient or by a member of the oxygen assessment team, depending on whether or not the patient was likely to be carrying the cylinder in day-to-day life. The flow rate used during the second test was decided using a semi-quantitative assessment of individual oxygen requirements, based on accumulated local experience. As an approximate guide, in patients of normal build, planning to carry their own cylinder, the required oxygen flow rate was estimated at 2 L·min^{-1} for desaturations of 86–88%, increasing by 1 L for every three percentage points of desaturation. Patients desaturating <70–75% were offered flow rates >6 L·min^{-1}. The estimated flow rate was increased by 25–50% in patients with body mass index (BMI) >30, while it was reduced by ~0.5 L if the oxygen cylinder was going to be carried by others. Ambulatory oxygen was provided as a continuous flow through nasal cannulae, except for six patients receiving ambulatory oxygen through a Venturi mask (40–60% oxygen).

Lung function tests performed within 3 months of the 6MWT were available for all patients. An echocardiogram performed

within 6 months of the 6MWT was available for 45 patients. Likely pulmonary hypertension was defined as an estimated pulmonary artery systolic pressure >40 mmHg.

Unless stated otherwise, values are expressed as mean±SE. Paired t-tests or Wilcoxon signed rank tests were used to compare outcome variables between the two 6MWTs, as appropriate. Chi-square analysis was used to compare frequency of binomial variables. Logistic regression models were used to compare baseline characteristics between patients stopping at least once during the first 6MWT and those completing both tests without stops.

Of the 52 patients, 32 were male, mean±SD age was 59.4±10.6 yrs, 30 were ex- or current smokers, mean forced vital capacity (FVC) was 58.1±18.7%, mean diffusing capacity of the lung for carbon monoxide ($D_{L,CO}$) was 25.6±8.3% and composite physiologic index (CPI) [6] was 63.4±8.9. Blood gas analysis was available for 36 patients, and mean arterial oxygen tension (P_{a,O_2}) was 8.4±1.6 kPa. Diagnoses included idiopathic fibrotic interstitial pneumonia (IIP) within the spectrum of idiopathic pulmonary fibrosis/fibrotic nonspecific interstitial pneumonia (n=34), ILD associated with a connective tissue disease (n=8), and fibrotic granulomatous disease (sarcoidosis or hypersensitivity pneumonitis; n=10). Likely pulmonary hypertension was present in 14 out of 45 patients (31.1%).

Compared to the baseline 6MWT, the use of (or increase in) ambulatory oxygen led to a highly significant increase in the average distance walked (255.1 *versus* 286.0 m; p<0.00001), S_{a,O_2} reached at the end of the test and to a significant decrease in the Borg dyspnoea score (table 1). Compared to the baseline test, significant reductions were also seen in the recovery time to pre-test levels in heart rate, in S_{a,O_2} and in Borg scores (table 1).

Out of 52 patients, 19 had to stop at least once during their baseline 6MWT, because of severe breathlessness and/or extreme fatigue. Of these, eight were able to complete the second 6MWT without stops (p<0.0001). Patients unable to complete the baseline 6MWT without stopping had a significantly lower P_{a,O_2}

TABLE 1 Change in 6-min walk test (6MWT) performance on ambulatory oxygen

	6MWT at baseline	6MWT on oxygen[#]	p-value
In all ILD patients[¶]			
Distance m	255.1±16.8	286.0±14.9	<0.00001
S_{a,O_2} end test %	76.3±1.1	84.7±1.1	<0.00001
Borg scale end test[+]	4.75 (4–5)	3.75 (3–4.3)	<0.00001
Heart rate end test	120.4±2.0	115.9±2.3	0.03
Heart rate recovery time s	218.5±19.9	145.5±10.4	<0.00001
Borg score recovery time s	185.3±21.2	133.7±12.8	0.0002
S_{a,O_2} recovery time s	183.6±20.2	102.7±8.5	<0.00001
In patients who completed both 6MWTs without stops[§]			
Distance m	318.9±15.4	332.3±15.1	0.002
S_{a,O_2} end test %	78.2±1.2	86.7±1.1	<0.00001
Borg scale end test[+]	4.0 (3–5)	3.5 (2.5–4)	<0.00001
Heart rate end test	118.6±2.6	112.5±3.1	0.04
Heart rate recovery time s	210.4±27.6	132.3±11.9	0.001
Borg score recovery time s	175.1±29.6	116.0±16.1	0.001
S_{a,O_2} recovery time s	162.2±24.2	83.8±8.3	0.0005
In patients who stopped at least once during the baseline 6MWT[ƒ]			
Distance m	144.2±19.2	205.6±21.2	0.0001
S_{a,O_2} end test %	73±2.0	81.3±2.0	<0.00001
Borg scale end test[+]	5 (4–6.7)	5 (3.3–6.0)	0.02
Heart rate end test	123.5±3.1	121.9±3.2	NS
Heart rate recovery time s	231.9±27.2	167.8±18.5	0.0007
Borg score recovery time s	203.2±27.4	164.5±19.6	0.07
S_{a,O_2} recovery time s	220.6±35.3	135.7±15.8	0.004
In fibrotic IIP patients[##]			
Distance m	272.3±19.8	304.7±17.8	0.0001
S_{a,O_2} end test %	75.6±1.1	83.4±1.3	<0.00001
Borg scale end test[+] median (95% CI)	4.25 (3–5)	3.25 (2.5–4)	<0.00001
Heart rate end test	119.6±2.5	116.6±3.0	NS
Heart rate recovery time s	214.3±25.9	138.1±12.4	0.0003
Borg score recovery time s	167.1±28.2	120.7±15.5	0.008
S_{a,O_2} recovery time s	177.4±24.2	104.0±10.5	0.0007

Data are presented as mean±SE unless stated otherwise. ILD: interstitial lung disease; S_{a,O_2}: arterial oxygen saturation; IIP: idiopathic fibrotic interstitial pneumonia; NS: nonspecific. [#]: additional or increased; [¶]: n=52; [+]: median (95% CI); [§]: n=33; [ƒ]: n=19; [##]: n=34.

compared to the rest (7.4±0.5 *versus* 8.8±0.3 kPa; p=0.01), a higher prevalence of pulmonary hypertension on echo (56.2% *versus* 17.2%; p=0.01), and tended to have a higher BMI (30.1±1.3 *versus* 27.7±0.9; p=0.1), while age, sex, FVC, $D_{L,CO}$ and CPI did not differ between the two groups. On logistic regression, the need to rest during the test remained linked to the presence of pulmonary hypertension (OR 10.4; p=0.006), even after adjusting for BMI; this finding remained robust after addition of age, sex and CPI to the model. When analysed separately (table 1), the average improvement in distance walked was significantly higher in patients who stopped at least once during their first test, compared to the others (mean improvement in distance of 61.4±12.5 *versus* 13.4±4.0 m; p=0.001), although a significant improvement in all outcome variables was also seen in the group completing both tests without stops (table 1).

The highly significant effects of ambulatory oxygen on 6MWD, end-test S_{a,O_2}, Borg score, and respective recovery times, were still observed when the analysis was restricted to the IIP subgroup (table 1), when the analysis was restricted to the patients whose initial 6MWT was performed on room air or to those who carried their own oxygen cylinder (n=36) (data not shown).

This retrospective study strongly suggests that ambulatory oxygen improves 6MWT performance in patients with ILD. The average improvement in 6MWD was 31 m, lying within the range recently reported as the clinically significant minimum important distance for patients with idiopathic pulmonary fibrosis [7, 8]. Our initial analysis included patients unable to complete the baseline 6MWT without stopping to rest at least once. The fact that a significant proportion of these were able to complete the second test without stops clearly suggests a positive effect of ambulatory oxygen. As could perhaps be expected, the improvement in 6MWD was particularly obvious in this group, although a significant improvement, to a lesser degree, was also seen in patients completing both tests without stopping. Interestingly, the main determinant of the need to stop was related to pulmonary vascular disease, but not to lung fibrosis severity, in keeping with the reported impact of pulmonary hypertension on exercise tolerance in fibrotic lung disease [9, 10].

The improvement in the 6MWT performance on ambulatory oxygen suggests that its use should be associated with increased mobility and quality of life. Whether this is the case will need to be assessed prospectively, also to assess whether potential improved mobility and reduced symptoms offset the disadvantages of ambulatory oxygen, including the psychological barriers to using oxygen devices in public and their relative cumbersomeness.

The study has several limitations, mostly due to its retrospective nature. Since patients did not perform a 6MWT on a placebo air cylinder, the benefits observed in subjective measures could, at least partially, be related to a placebo effect. However, the more objective improvements in outcomes such as oxygen saturation and heart rate, and time to recovery to their respective baseline levels, are unlikely to be solely placebo-related. Furthermore, the oximeter was not readily visible to the patient while performing the 6MWT, and no information was given regarding any physiological variables until the test was completed.

The baseline test was not repeated to assess intrinsic variability. However, an excellent short-term reproducibility has been described for the 6MWD in fibrotic IIP patients [1], with good reproducibility for the pre- and post-test Borg score, while oxygen desaturation was subject to greater variability. A training effect on the second test cannot be completely discounted. However, the small benefits associated with a training effect of a single repeat test [3] are likely to have been offset by the increased work of carrying the oxygen cylinder in the second test, as was the case for approximately two-thirds of patients and, therefore, seems unlikely to have been a significant confounding factor. Finally, this group of patients had quite severe lung involvement, as shown by baseline $D_{L,CO}$ and extent of oxygen desaturation on walking; whether the benefits of ambulatory oxygen can also be seen in ILD patients with milder oxygen desaturation on exercise remains to be evaluated.

In conclusion, this study suggests that ambulatory oxygen significantly improves 6MWD, oxygen saturation and dyspnoea score in ILD patients. Further studies are needed to assess optimal criteria for prescribing ambulatory oxygen in ILD patients, to assess whether they differ according to type of ILD, and to evaluate the impact of ambulatory oxygen on patients' quality of life and day-to-day activities.

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Statement of Interest: None declared.

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DOI: 10.1183/09031936.00190710