Prognostic Value of Desaturation during a 6-Minute Walk Test in Idiopathic Interstitial Pneumonia

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Exercise-induced hypoxia is an index of the severity of interstitial lung disease. We hypothesized that desaturation during a 6-minute walk test would predict mortality for patients with usual interstitial pneumonia (n = 83) and nonspecific interstitial pneumonia (n = 22). Consecutive patients with biopsy-proven disease performed a 6-minute walk test between January 1996 and December 2001. Desaturation was defined as a fall in oxygen saturation to 88% or less during the 6-minute walk test. Desaturation was common (44 of 83 usual interstitial pneumonia and 8 of 22 nonspecific interstitial pneumonia; chi square, p = 0.39). Patients with usual interstitial pneumonia or nonspecific interstitial pneumonia who desaturated had a significantly higher mortality than patients who did not desaturate (respective log-rank tests, p = 0.0018, p = 0.0089). In patients with usual interstitial pneumonia, the presence of desaturation was associated with an increased hazard of death (hazard ratio, 4.2; 95% confidence interval, 1.40, 12.56; p = 0.01) after adjusting for age, sex, smoking, baseline diffusion capacity for carbon monoxide, FVC, and resting saturation. We conclude that knowledge of desaturation during a 6-minute walk test adds prognostic information for patients with usual interstitial pneumonia and nonspecific interstitial pneumonia.

Keywords: 6-minute walk test; usual interstitial pneumonia; nonspecific interstitial pneumonia

As a group, patients with usual interstitial pneumonia (UIP) have a poor prognosis (a median survival of 2.8 to 4.0 years) (1–4). The prognosis for any individual patient, however, is variable. As such, additional predictors of survival are important to help patients and physicians stratify the risks and benefits of therapeutic endeavors, including experimental protocols, cytotoxic therapies, and lung transplantation. Recent studies have identified demographic (age, smoking, sex), physiologic (diffusion capacity for carbon monoxide [D_{LCO}], FVC, exercise Pa_{O_2}), radiographic (amount of fibrosis), and histopathologic features (fibroblastic foci) that are associated with survival (2, 5–11).

A central feature in the pathophysiology of idiopathic pulmonary fibrosis (IPF) is impaired gas exchange that worsens with exercise (1, 12). Exercise-induced widening of alveolar arterial O_2 gradient and a fall in arterial Po_2 are secondary to multiple abnormalities, including ventilation/perfusion mismatching, O_2 diffusion limitation, low mixed venous Po_2, and right-to-left intracardiac shunting through a patent foramen ovale (13–17). Pa_{O_2} with exercise (2) and at rest (18) has been shown to predict survival in patients with UIP.

A simple test to evaluate desaturation with exertion is a 6-minute walk test (6MWT) (19, 20). Desaturation of hemoglobin, as measured by pulse oximetry, during a 6MWT is predictive of mortality in patients with primary pulmonary hypertension (21). We hypothesized that desaturation during a 6MWT would provide additional prognostic information regarding survival for patients with UIP and nonspecific interstitial pneumonia (NSIP) after accounting for demographic, physiologic, and radiographic features. Some of the results of this study have been reported in the form of an abstract (22).

METHODS

Patient Selection

Consecutive patients with surgical lung biopsy–confirmed UIP and NSIP who underwent a 6MWT on room air between January 1996 and December 2001 formed the study group. This study used patients from the University of Michigan Specialized Center of Research in the Pathobiology of Fibrotic Lung Disease database. The slides were reviewed by two independent pathologists, and the diagnoses of UIP and NSIP were based on American Thoracic Society/European Respiratory Society guidelines (23). Patients with underlying collagen vascular disease or occupational exposure were excluded. A subgroup of these patients has been previously described (7). Approval for the use of these data was obtained from the Institutional Review Board of the University of Michigan.

Pulmonary Function Testing and High-resolution Computed Tomography

Pulmonary function tests, including spirometry and D_{LCO}, were performed as previously described (24). High-resolution computed tomography examinations were performed and semiquantitatively scored for ground-glass opacity and interstitial opacity (computed tomography fibrosis score [CT-fib]) as previously described (7, 25). The radiologists were unaware of the histologic diagnosis at the time of interpretation.

6MWT

The protocol used for the 6MWT was designed to ensure an accurate assessment of oxygen desaturation and to provide a clinically useful oxygen titration. All patients were tested under standardized conditions in the same pulmonary function laboratory by trained technicians who were blinded to the histologic diagnosis. Baseline blood pressure, heart rate, and oxygen saturation using Nellcore pulse oximetry (Nellcore N-3000; Mallinckrodt Inc., Hazelwood, MO) were measured. If the resting saturation was less than 88% on room air, patients were not considered eligible for room air 6MWT. These patients were excluded from the study group.

Patients were instructed as follows: "The object of this test is to walk as quickly as you can for 6 minutes to cover as much ground as possible. You may slow down if necessary. If you stop we wish you to continue the walk again as soon as possible. Your goal is to walk as fast and as far as you can in 6 minutes." To ensure an accurate assessment of the oxygen saturation, the respiratory therapist checked that the pulse

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oximeter had an acceptable signal and that the oximeter bar was pulsing to show the heart rate and was in synchrony with the heart rate before beginning all tests. Fingernail polish, if worn by the patient, was removed before testing. Patients walked on a level surface with gentle encouragement using set phrases every 30 seconds. Sa_{O_2} was measured continuously during the walk. If the patient experienced an oxygen saturation of 88% persistent for 1 minute or if saturation fell below 87%, the study was repeated with supplemental oxygen administered using a threshold similar to that of other investigators in this field (26, 27) and following published recommendations (28). Maximal distance was defined as the maximal achieved walk distance during room air or oxygen-supplemented 6MWT.

Statistical Analysis

Categorical data were compared using chi-square tests (29), and continuous data were compared using two-tailed *t* tests (30). All *t* tests assumed unequal variances with p values of less than 0.05 considered statistically significant. Vital status, ascertained as of June 2002, was determined by review of electronic patient charts and review of the most recent social security death index. Survival experiences for desaturation status groups were illustrated via Kaplan-Meier curves (31). Four patients underwent lung transplantation and were censored on the date of transplantation. Cox regression analysis (32) was used to examine the relationship between desaturation and mortality, adjusting for demographic characteristics (age, sex, and smoking status), physiologic data (FVC, D_{LCO}, resting Sa_{O_2}) and radiographic variables (CT-fib). For the purpose of data analysis, desaturation was defined as fall in Sa_{O_2} equal to or below 88% during the room air 6MWT (27, 28). Additional analyses were performed with decrease in saturation (Δ sat = resting saturation − lowest saturation on 6MWT) expressed as a continuous variable or as a 4% decrease from the baseline saturation (Δ sat of 4% or more). A logistic regression analysis (33) was used to determine whether baseline demographic, physiologic, radiographic, or histopathologic information could predict desaturation.

RESULTS

Of the 123 patients who underwent 6MWT during the study period, 18 (UIP = 15, NSIP = 3) were excluded, as their resting saturations were less than 88%, and hence, they did not undergo a room air 6MWT. One hundred and five patients (UIP = 83, NSIP = 22) made up the study group. Table 1 compares the physiologic and walk test characteristics seen in the two cohorts. Thirty-eight UIP and eight NSIP patients met criteria for oxygen supplementation.

A similar proportion of patients with UIP (44 of 83, 53%) and NSIP (8 of 22, 36%) desaturated (chi square, p = 0.17). No significant differences were noted in age, sex, smoking history, or treatment given between patients with UIP or NSIP who desaturated versus those that did not desaturate. Similarly, there was no significant difference in the interval between open lung biopsy and walk test between those who desaturated versus those that did not desaturate (mean biopsy–walk interval: desaturators 7.84 ± 18.01 months [n = 52], nondesaturators 7.67 ± 16.09 months [n = 53], p = 0.95). Patients with UIP who desaturated exhibited significantly lower values of FVC, D_{LCO}, and resting saturation than patients with UIP who did not desaturate. No significant difference in pulmonary function was noted between patients with NSIP who did and did not desaturate, although there was a trend toward a lower D_{LCO} in the group that desaturated. The small number of patients with NSIP may have limited our ability to detect statistically significant differences. Resting saturation was significantly lower in patients with NSIP that desaturated (Table 2).

TABLE 1. PHYSIOLOGIC AND 6-MINUTE WALK TEST FEATURES OF PATIENTS WITH USUAL INTERSTITIAL PNEUMONIA AND NONSPECIFIC INTERSTITIAL PNEUMONIA

Characteristic	UIP (*n = 83*)	NSIP (*n = 22*)	p Value
Resting saturation, %	95.6 ± 1.0	96.0 ± 2.5	0.48*
Δ Saturation, % points	7.1 ± 4.1	5.7 ± 4.1	0.17*
Desaturation	44 (53%)	8 (36%)	0.17†
Δ Saturation ⩾ 2%	75 (90%)	20 (90%)	0.94†
Δ Saturation ⩾ 4%	66 (80%)	14 (64%)	0.12†
Maximal distance, ft	1,166 ± 355	1,174 ± 313	0.92*

Definition of abbreviations: desaturation = oxygen saturation of 88% or less on the 6MWT; NSIP = nonspecific interstitial pneumonia; Δ saturation = resting saturation − lowest saturation on 6MWT; UIP = usual interstitial pneumonia.

* *t* test (unequal variances).

† χ^2 test.

D_{LCO} (odds ratio of 0.50 for a 10-unit increase in D_{LCO} percentage predicted; 95% confidence interval [CI], 0.32–0.78; p = 0.002) and resting saturation (odds ratio of 0.41 for 1% increase in resting saturation; 95% CI, 0.41–0.87; p = 0.0066) were significant predictors of desaturation after adjusting for age, sex, smoking history, CT-fib score, and FVC in patients with UIP. No significant predictors of desaturation were identified in the group with NSIP.

The median follow-up period was 2.93 years (range of 0.1 to 5.7 years) in the UIP group and 3.63 years (0.32 to 5.6 years) in the NSIP group. Patients with UIP or NSIP who desaturated had a significantly higher mortality than patients that did not desaturate (log-rank test, p = 0.0018, p = 0.0089) (Figures 1 and 2). The 4-year survival rate was higher in the group that did not desaturate on 6MWT (Table 3).

Univariate analysis was performed using variables that have been suggested to influence survival in previous studies of patients with UIP (Table 4). The lack of deaths in the patients with NSIP who did not desaturate precluded further analysis in this subset of patients. The presence of desaturation (hazard ratio [HR], 3.25; 95% CI, 1.47–7.2; p = 0.0016), lower FVC (HR for a 1-L increase, 0.65; 95% CI, 0.42–1.00; p = 0.05), and lower FEV_1 (HR for a 1-L increase 0.58; 95% CI, 0.33–0.99; p = 0.04) were found to be significant predictors of mortality. Importantly, after adjusting for age, sex, smoking history, baseline D_{LCO} percent predicted, FVC percent predicted, resting saturation, and histologic diagnosis, desaturation on 6MWT remained a significant predictor of mortality in all patients (UIP and NSIP) (HR, 4.47; 95% CI, 1.58–12.64; p = 0.005) (Table 5) and when the analysis was repeated only in UIP patients (HR, 4.20; 95% CI, 1.40–12.56; p = 0.01) (Table 5). The strength of this association was maintained after adjusting for high-resolution computed tomography fibrotic scores (data not shown).

In additional analyses, we examined alternative approaches to defining a fall in saturation during a 6MWT; Δ saturation (resting saturation − lowest saturation on 6MWT as a continuous parameter) was a significant predictor of mortality in both univariate (HR, 1.18; 95% CI, 1.08–1.28; p = 0.003) and multivariate analysis (HR, 1.23; 95% CI, 1.08–1.40; p = 0.0004). For each percentage decrease in saturation, mortality increased by 23%. As others have suggested that a decrease in saturation of 4% is clinically significant (1, 34), we explored this threshold. A decrease in saturation of 4% or more (Δ saturation of four or more) was a significant predictor of mortality in multivariate analysis (HR, 13.58; 95% CI, 1.71–107.54; p = 0.01).

DISCUSSION

In this study, we examined the relationship between desaturation during a 6MWT and survival in patients with UIP and NSIP. We found that desaturation was strongly predictive of mortality. In patients with UIP, after adjusting for age, sex, smoking history, baseline D_{LCO} percent predicted, FVC percent predicted, resting

TABLE 2. DEMOGRAPHIC, PHYSIOLOGIC, AND HIGH-RESOLUTION COMPUTED TOMOGRAPHY FEATURES OF USUAL INTERSTITIAL PNEUMONIA AND NONSPECIFIC INTERSTITIAL PNEUMONIA

	Usual Interstitial Pneumonia			Nonspecific Interstitial Pneumonia		
Variable	No Desaturation, n = 39 (*mean* ± *SD*)	Desaturation, n = 44 (*mean* ± *SD*)	p Value	No Desaturation, n = 14 (*mean* ± *SD*)	Desaturation, n = 8 (*mean* ± *SD*)	p Value
Demographics						
Age, yr	63 ± 11	61 ± 9	0.29†	57 ± 9	61 ± 10	0.33†
Sex, male/female	20/19	24/20	0.76‡	8/6	6/2	0.40‡
Smokers, %	69	68	0.92‡	64	63	0.93‡
Cigarette consumption, pack years	24 (4–92)*	21.5 (4–80)*	0.54†	33 (7–90)*	36 (14–53)*	0.78†
Treatment			0.79‡			0.19‡
No treatment	3	1		2	1	
Prednisone	6	8		4	3	
Prednisone + azathioprine	16	17		5	0	
Azathioprine	12	14		2	2	
Miscellaneous	2	4		1	2	
Physiologic						
FVC, L	2.60 ± 0.93	2.13 ± 0.61	0.0096†	2.52 ± 0.88	3.09 ± 0.72	0.12†
FVC, % predicted	71 ± 21	58 ± 16	0.0055†	68 ± 23	74 ± 14	0.51†
FEV_1, L	2.17 ± 0.75	1.80 ± 0.49	0.0089†	1.93 ± 0.66	2.33 ± 0.47	0.11†
FEV_1, % predicted	83 ± 24	68 ± 17	0.0027†	70 ± 22	79 ± 15	0.31†
$D_{L_{CO}}$ ml/min/mm Hg	15.00 ± 5.33	10.42 ± 3.22	< 0.0001†	13.73 ± 4.66	10.98 ± 3.90	0.16†
$D_{L_{CO}}$, % predicted	59 ± 18	42 ± 12	< 0.0001†	57 ± 22	42 ± 13	0.06†
Resting saturation, %	96.31 ± 1.76	94.95 ± 2.03	< 0.0017†	97 ± 1.66	94.3 ± 2.76	0.03†
HRCT						
CT-fib score	1.68 ± 0.55	1.78 ± 0.76	0.50†	1.16 ± 0.82	0.98 ± 0.64	0.64†

Definition of abbreviations: CT-fib = semiquantitatively scored interstitial opacity on high-resolution computerized tomography (25); $D_{L_{CO}}$ = carbon monoxide diffusion capacity; HRCT = high-resolution computerized tomography; NSIP = nonspecific interstitial pneumonia; UIP = usual interstitial pneumonia.

* Median (range).

† *t* test (unequal variances).

‡ χ^2 test.

Patients are stratified by the presence or absence of desaturation (oxygen saturation OF 88% or less) on a 6-minute walk test.

saturation, and the amount of fibrosis on high-resolution computed tomography, the presence of desaturation was associated with a greater than fourfold hazard of death. Furthermore, all deaths in patients with NSIP occurred in patients who desaturated. We also demonstrate that desaturation is frequently noted in both patients with UIP (44 of 83, 53%) and NSIP (8 of 22, 36%). A significant predictor of desaturation in patients with UIP was $D_{L_{CO}}$ after adjusting for age, sex, smoking history, FVC, and the amount of fibrosis on high-resolution computed tomography.

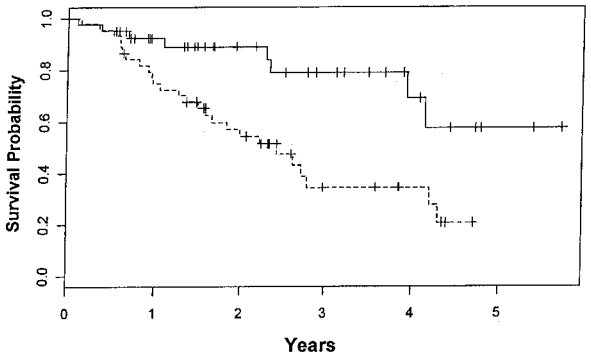

Figure 1. Kaplan-Meier survival curve for patients with usual interstitial pneumonia (UIP) grouped by desaturation (oxygen saturation of 88% or less) on 6MWT (desaturators, *dashed line*; nondesaturators, *solid line*; p = 0.0018).

Our data demonstrate that UIP patients who desaturate during a 6MWT had a more than fourfold higher hazard of dying during follow-up. The prognostic importance of exercise-induced hypoxia has been suggested in the literature (2, 35). In the clinical radiologic physiologic scoring system devised to predict survival in IPF, resting gas exchange was not important; however, exercise Pa_{O_2} on cardiopulmonary exercise testing was significantly predictive of survival and accounted for as much as 10.5% of the maximum in predicting survival (2). More recently, in a study of 41 patients with IPF, exercise induced hypoxemia evaluated by $\Delta Pa_{O_2}/\Delta \dot{V}o_2$ on cardiopulmonary exercise testing was strongly correlated with survival (35). Importantly, other investigators have not confirmed that cardiopulmonary exercise testing measures of gas exchange provide additional prognostic value in IPF patients (24, 36). Furthermore, registry data suggest that exercise testing is infrequently used in clinical practice to evaluate patients with IPF (37). This may relate to the expense and limited availability of this diagnostic modality. In contrast, 6MWT is a simple, inexpensive test that is convenient, requires minimal medical personnel, and can be performed in an office setting (28). Moreover, a good correlation has been demonstrated between O_2 uptake and peak Pa_{O_2} between cardiopulmonary exercise testing and 6MWT (38). Furthermore, in a study of 80 consecutive patients with COPD, 6MWT was found to be more sensitive than maximal incremental cycle testing in detecting desaturation defined as fall in saturation of 4% or more by pulse

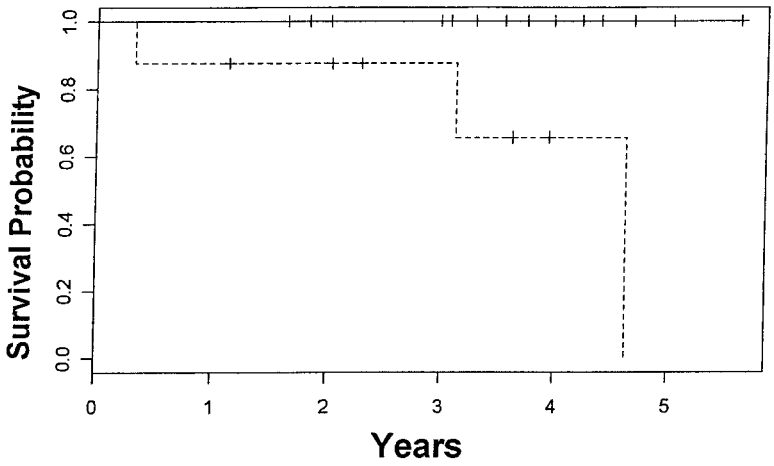

Figure 2. Kaplan-Meier survival curve in patients with nonspecific interstitial pneumonia (NSIP) grouped by desaturation (oxygen saturation of 88% or less) on 6MWT (desaturators, *dashed line*; nondesaturators, *solid line*; p = 0.0089).

oximetry (34). These investigators also confirmed the reproducibility of changes in pulse oximetry on repeat 6MWTs. This is not surprising, as pulse oximetry has been found to be accurate within 2% (±1 SD) or 5% (±2 SD) of *in vitro* oximetry in the range of 70% to 100% Sa_{O_2} (39). Our data demonstrate that desaturation on 6MWT in patients with UIP and NSIP portends a bad prognosis and provides compelling support for the routine use of this technique in patients with UIP and NSIP.

We demonstrate a strong correlation of measures of fall in saturation on a 6MWT and survival independent of the format used to define desaturation. A decrease in saturation below 88% has been used by others examining gas exchange in interstitial disease (27) and to identify patients requiring oxygen supplementation during exercise (28). Importantly, the use of this threshold in our data set provides two equally distributed groups with very different survival rates. The 4-year survival rate of UIP patients who desaturated to this level was 34.5% compared with 69.1% in patients who did not desaturate. The use of a change in saturation as a continuous variable confirms the strong predictive ability of desaturation during 6MWT to predict a less favorable outcome; for each 1% decrease in saturation, mortality increased by 23%. A recent American Thoracic Society consensus statement suggested a 4% decrease in saturation during exercise as an adverse prognostic sign in IPF (1). Our data provide support for this, as patients experiencing such a level of desaturation exhibited a nearly 14-fold increase in mortality, albeit with a wide confidence interval. The latter likely reflects that most patients in the current cohort experienced a decrease in saturation of 4% or more, with only one death noted in the 17 patients who exhibited a decrease in saturation of less than 4%. These data provide a compelling argument for the clinical use of the 6MWT in the evaluation of patients with UIP and NSIP. As the 4-year survival after lung transplantation in IPF patients is approximately 45% (40), a strong case can be made for referring UIP patients who meet published criteria (41) and who desaturate during 6MWT. As UIP patients who desaturate experience a 4-year survival of 34.5%, they are most likely to experience a survival benefit from lung transplantation. In contrast, UIP patients who do not desaturate during 6MWT experience a 4-year survival of 69.1%, suggesting that a delay in listing may not impair long-term survival in this group.

D_{LCO} was a predictor of desaturation on 6MWT in UIP patients but did not correlate with mortality in multivariate models. The prognostic value of the simple 6MWT likely reflects the cumulative impact of ventilation/perfusion mismatching, O_2 diffusion limitation, low mixed venous Po_2, and right-to-left intracardiac shunting through a patent foramen ovale that may be seen in patients with fibrotic lung diseases (13–17). Several authors have suggested a fair correlation between measures of gas exchange during maximal exercise testing and the extent of physiologic or radiologic abnormality in patients with pulmonary fibrosis (42–49). Some have documented modest correlations between static physiologic parameters and desaturation during 6MWT (50) in patients with interstitial lung diseases. Arterial oxygen tension during maximal exercise has been correlated

TABLE 3. FOUR-YEAR SURVIVAL RATE FOR PATIENTS WITH NONSPECIFIC INTERSTITIAL PNEUMONIA AND USUAL INTERSTITIAL PNEUMONIA

	4-Year Survival Rate	95% CI
UIP no desaturation	69.1%	46.2–91.9%
UIP desaturation	34.5%	17.4–51.7%
NSIP no desaturation	100%	—
NSIP desaturation	65.6%	24.7–100%

Definition of abbreviations: CI = confidence interval; NSIP = nonspecific interstitial pneumonia; UIP = usual interstitial pneumonia.

Patients are stratified by the presence or absence of desaturation (oxygen saturation of 88% or less) on a 6-minute walk test.

TABLE 4. UNIVARIATE ANALYSIS OF SURVIVAL IN PATIENTS WITH USUAL INTERSTITIAL PNEUMONIA

Parameter	Hazard Ratio (*95% CI*)	p Value
Demographic age, yr	1.00 (0.97–1.04)	0.81
Male sex	1.05 (0.53–2.08)	0.89
Positive smoking history	0.62 (0.31–1.24)	0.18
Physiology FVC, L	0.65 (0.42–1.00)	0.05
FVC, per 10% predicted	0.84 (0.69–1.00)	0.06
FEV_1, L	0.58 (0.33–0.99)	0.04
FEV_1, per 10% predicted	0.86 (0.73–1.01)	0.07
D_{LCO} ml/min/mm Hg	0.95 (0.87–1.03)	0.21
D_{LCO}, per 10% predicted	0.85 (0.68–1.06)	0.13
Timed walk test desaturation	3.25 (1.47–7.20)	0.0016
Resting saturation	0.91 (0.77–1.08)	0.27
Maximal distance, per 10 ft	0.997 (0.989–1.006)	0.53
HRCT CT-fib	1.23 (0.73–2.07)	0.43

Definition of abbreviations: CI = confidence interval; CT-fib = semiquantitatively scored interstitial opacity on high-resolution computerized tomography (25); desaturation = oxygen saturation of 88% or less on 6MWT; D_{LCO} = carbon monoxide diffusion capacity; UIP = usual interstitial pneumonia.

TABLE 5. MULTIVARIATE ANALYSIS OF SURVIVAL

Parameter	Hazard Ratio (*95% CI*)	p Value
All patients		
Age, yr	1.04 (0.99–1.09)	0.09
Male sex	1.18 (0.53–2.63)	0.69
Positive smoking history	0.88 (0.39–1.98)	0.76
D_{LCO}, per 10% predicted	1.04 (0.76–1.42)	0.81
FVC, per 10% predicted	0.86 (0.68–1.08)	0.20
UIP	3.14 (0.91–10.92)	0.07
Resting saturation	0.96 (0.79–1.17)	0.67
Desaturation	4.47 (1.58–12.64)	0.005
UIP patients		
Age, yr	1.04 (0.98–1.09)	0.16
Male sex	1.13 (0.49–2.58)	0.78
Positive smoking history	0.79 (0.35–1.83)	0.59
D_{LCO}, per 10% predicted	1.11 (0.80–1.55)	0.53
FVC, per 10% predicted	0.85 (0.67–1.07)	0.17
Resting saturation	1.03 (0.82–1.23)	0.97
Desaturation	4.20 (1.40–12.56)	0.01

Definition of abbreviations: CI = confidence interval; desaturation = oxygen saturation of 88% or less on 6MWT; D_{LCO} = carbon monoxide diffusion capacity; UIP = usual interstitial pneumonia.

with D_{LCO} in patients with IPF (51–53). Given the prognostic value of exercise desaturation in patients with primary pulmonary hypertension (21), it may be that the additional value afforded by a measurement of exercise induced desaturation in UIP and NSIP reflects the contribution of pulmonary hypertension that is frequently noted in fibrotic lung disease (54). The simplicity of the 6MWT and its probable ability to assess complex physiologic interactions and predict prognosis make the 6MWT an important tool for the management of patients with IPF.

Another novel finding of this study is the documentation that a fall in saturation during 6MWT is a very common phenomenon in patients with UIP and NSIP. Ninety percent of the patients with UIP and NSIP had a fall in saturation of 2% or more, and desaturation to 88% or less was seen in approximately 50% and 36% of patients with UIP and NSIP, respectively. Gas exchange during exercise has been suggested as an important pathophysiologic abnormality in patients with idiopathic interstitial pneumonia (1, 12). Although most of the studies evaluating exercise-induced desaturation have used cardiopulmonary exercise testing, two recent studies have examined saturation during a 6MWT in patients with interstitial lung disease. Desaturation to 88% or less was seen in 38% of patients with interstitial lung diseases (33 of 50 with IPF) on a 6MWT (27). Similarly, in a study of 40 patients with varying interstitial lung diseases (19 IPF patients), eight patients exhibited a drop of 2–5%, whereas 16 experienced desaturation of more than 5% on a 6MWT (50). Importantly, our study examines a large number of patients with specific histologic diagnoses and confirms that desaturation on a 6MWT is a common finding in patients with UIP and NSIP.

Another interesting finding of our study was that no difference was seen in the frequency and degree of fall in saturation during a 6MWT in patients with UIP and NSIP. Some investigators have suggested a greater rise in the alveolar arterial O_2 during exercise in patients with UIP compared with desquamative interstitial pneumonia, asbestosis, berylliosis, sarcoidosis, or α-1 antitrypsin–related emphysema (53, 55). In contrast, the trough saturation was similar in a retrospective series of patients with NSIP (n = 14) compared with UIP (n = 63); the mode of exercise testing or proportion with desaturation was not described (3). In our study, we found no statistical difference in any of the variables obtained during a 6MWT, including resting saturation, various degrees of fall in saturation, and maximal distance walked in patients with NSIP and UIP. Together, these studies suggest that desaturation on 6MWT in patients with UIP and NSIP is seen more frequently than other pulmonary diseases and occurs with similar frequency in patients with UIP and NSIP.

In conclusion, desaturation during a 6MWT is a strong predictor of mortality in patients with UIP and NSIP. This effect persists after adjustment for patient demographic factors, static physiologic testing, and the amount of fibrosis on high-resolution computed tomography. This simple exercise modality, which can be easily obtained in an outpatient setting at a low cost, may be particularly important in prognostication in patients with UIP and NSIP and may help optimize referral and listing of patients for lung transplantation. Our data also suggest that desaturation on a 6MWT could be used for stratification of patients with UIP in clinical trials, as these two groups exhibit a very different survival profile. Further research is required to determine the role of serial measures of 6MWT in the follow-up of patients with UIP and whether desaturation on a 6MWT can be used as a surrogate for survival in phase II trials. Although 6MWT has been suggested as a measure of functional capacity with distance as the primary endpoint, our data confirm that documentation of desaturation offers important information in patients with UIP and NSIP.

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