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# The timed walk test as a measure of severity and survival in idiopathic pulmonary fibrosis

**T.S. Hallstrand*, L.J. Boitano*, W.C. Johnson#, C.A. Spada*, J.G. Hayes* and G. Raghu***

**ABSTRACT: Idiopathic pulmonary fibrosis (IPF) is a relentlessly progressive disease with a median survival of ~3 yrs. Measurements of airflow and lung volumes at rest are generally used to monitor the clinical course in this disorder. This study was designed to determine if a modified version of the 6-min walk test, called the timed walk test, accurately characterises disease severity and survival in IPF.**

**The study population consisted of 28 patients with well-characterised progressive IPF. The timed walk test and concurrent measures of disease severity were assessed at baseline. Participants were prospectively followed for ⩾4 yrs to determine the relationship between parameters of the timed walk test and survival.**

**There were strong correlations between the end-exercise saturation and walk-velocity parameters of the timed walk test and diffusing capacity, and arterial oxygen tension at rest. In univariate Cox proportional-hazards models, end-exercise saturation, change in saturation with exercise, walk distance and walk velocity were associated with survival. In unadjusted logistic regression models, odds of death at 2 yrs were associated with the same parameters.**

**In conclusion, the timed walk test relates to disease severity and long-term outcome in progressive idiopathic pulmonary fibrosis.**

**KEYWORDS: Idiopathic pulmonary fibrosis, interstitial lung disease, pulmonary function, survival, walk test**

AFFILIATIONS
*Dept of Medicine, Division of Pulmonary and Critical Care Medicine, and
#Dept of Biostatistics, University of Washington, Seattle, WA, USA.

CORRESPONDENCE
G. Raghu
Chest Clinic
Interstitial Lung Disease
Sarcoid and Pulmonary Fibrosis Program
University of Washington Medical Center
Box 356522
BB-1253 HSC
1959 NE Pacific Street
Seattle,
WA 98195-6522
USA
Fax: 1 2066858673
E-mail: graghu@u.washington.edu

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Idiopathic pulmonary fibrosis (IPF) is a chronic progressive interstitial lung disease (ILD) of unknown cause, resulting in severe morbidity and death due to progressive respiratory failure [1], usually within 3–5 yrs [2–5]. Prognostic factors that have been variably associated with survival include age [6], smoking status [7], sex [8], resting pulmonary function [9], histopathology score [7], fibrotic score based on high-resolution computed tomography [10, 11], and initial response to treatment with corticosteroids [10]. A composite score of clinical, radiographical and physiological variables has been associated with survival in IPF [12]. Survival is the most important treatment outcome in IPF, but requires large numbers of patients with this rare disease for long periods (*i.e.* 3–5 yrs) of prospective follow-up. A measurement of disease and functional status that can serve as a surrogate outcome measurement to accurately reflect the risk of progression to death in IPF is needed.

A practical and simple measurement of functional status that is widely used as a clinical tool and outcome measure of patients with heart [13], obstructive lung disease [14], vascular [15], and neuromuscular disease [16] is the 6-min walk test (6MWT). However, the physiological abnormalities associated with disease severity and progression in IPF are not fully characterised by the distance of the 6MWT [7, 9, 12]. This was illustrated recently in the study by LAMA *et al*. [17], which showed that, in a subgroup of patients with IPF without resting hypoxaemia, the 6MWT distance was not associated with survival [17]. Cardiopulmonary exercise tests have shown that changes in arterial saturation and exercise performance are related to survival in IPF, leading to the hypothesis in the current study that similar parameters assessed during a self-paced walk test would be associated with survival. Therefore, a modified version of the 6MWT, the timed walk test (TWT), was developed as a clinical tool and outcome measurement in IPF. The TWT has three stopping criteria so that continuous walk velocity can be assessed and to incorporate change in oxyhaemoglobin saturation during continuous exercise. To make the test applicable to patients with a range of disease severity and to reduce the influence of hypoxaemia on walk velocity [18, 19], the TWT was conducted in room air in patients with a baseline saturation >88% and on supplemental

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oxygen if baseline saturation was <88%. In this study, the relationship between the TWT and concurrent measures of disease severity conventionally used in IPF was evaluated. Participants were prospectively followed for ⩾4 yrs to determine the relationship between parameters of the TWT and survival.

## METHODS

### Study population

A prospective study of consecutive new referrals for further management of IPF (referred to the Interstitial Lung Disease Clinic, University of Washington Medical Center, Seattle, WA, USA, and for further evaluation and management in the Interstitial Lung Disease/Sarcoid/Pulmonary Fibrosis Program at the University of Washington under the direction of G. Raghu) was initiated between 1996 and 1998. Patients were included in this study if they consented to the study and met the diagnostic criteria for IPF. The diagnosis of IPF was ascertained by typical clinical, radiographical, nondiagnostic transbronchial biopsy, and physiological features consistent with IPF; surgical lung biopsy demonstrating histological features of usual interstitial pneumonia was accepted for the diagnosis of IPF in patients not meeting the major and minor clinical criteria [1, 20]. Persons with collagen vascular disease, occupational lung disease, sarcoid, hypersensitivity pneumonitis and other idiopathic interstitial pneumonias were excluded [1, 21]. Patients with concurrent emphysema were excluded based on elevated residual volume of ⩾120% and forced expiratory volume in one second ($FEV_1$)/forced vital capacity (FVC) ratio of ⩽0.60. Patients with IPF who were entered into this study had progressive symptomatic and/or physiological deterioration [1], despite treatment with prednisone with or without immunosuppressives. The University of Washington Human Subjects Review Committee approved the study, and each participant gave written informed consent.

### Timed walk test

A designated respiratory therapist (L.J. Boitano) conducted the TWT on a 30-m-long level course marked in 1.5-m increments. Oxygen saturation was recorded continuously by pulse oximetry at rest for 5 min prior to the test, throughout the TWT and immediately after the test. Patients with resting room air saturation >88% had an initial walk test in room air and were subsequently asked to perform a second test on 2 L of oxygen. Patients with resting saturation ⩽88% were tested only on 2 L of oxygen after a 5-min period of supplemental oxygen at rest. During the TWT, patients were instructed to walk at a pace comfortable to them until they became too fatigued, up to a maximum of 6 min. The respiratory therapist stopped the test if the patient demonstrated signs of overt fatigue and/or asked to stop, or the saturation dropped to <80%. Although the test was stopped when saturation reached 80%, the lowest saturation was recorded if the saturation continued to decline. The distance, time and saturation were recorded at the end of the test. The primary parameters of the TWT were the end-exercise saturation, change in saturation from baseline and walk velocity. Secondary parameters were walk distance and walk time.

### Pulmonary function testing

Spirometry, plethysmographic lung volumes and diffusing capacity for carbon monoxide ($D_{L,CO}$) were performed within 24 h of the TWT, according to American Thoracic Society standards [22]. Arterial blood gases were obtained after 5 min of inactivity. The alveolar–arterial oxygen tension ($P_{A-a,O_2}$) difference was calculated by the alveolar gas equation [23].

### Statistical analysis

Relationships between parameters of the TWT and pulmonary function were assessed with Spearman rank correlation coefficients. Least squares linear regression was used to further delineate the association between $D_{L,CO}$ and the TWT parameters. An intraclass correlation coefficient was used to assess the repeatability of the TWT.

Survival time was measured in days from enrolment until death or censoring. Patients were censored at the end of the follow-up period or if they underwent lung transplantation. Univariate Cox proportional-hazards models assessed the relative hazard corresponding to overall mortality for each TWT parameter. Cox proportional-hazards models were subsequently adjusted for supplemental oxygen to assess its effect on each TWT parameter in predicting survival. The effects of other demographic and baseline variables on TWT parameter estimates of survival were also explored using multivariate Cox proportional-hazards models. Kaplan–Meier estimates of survival were used to illustrate the findings of the Cox model. Logistic regression models of TWT parameters predicting 2-yr survival were used to corroborate findings of the survival analyses.

## RESULTS

### Study participants

A total of 28 consecutive patients with IPF [1] were enrolled in the study (table 1). Disease severity ranged from FVC ⩾70% pred in eight patients and ⩽40% pred in five. All patients had progressive disease based on symptoms or pulmonary function tests, despite treatment with prednisone with or without azathioprine [1].

### Characteristics of the timed walk test

At entry, nine of the 28 participants had resting oxyhaemoglobin saturations ⩽88% and, therefore, were only tested on 2 L of supplemental oxygen. Six of these nine participants who were tested on supplemental oxygen stopped prior to 6 min because arterial oxygen saturation measured by pulse oximetry ($S_{P,O_2}$) reached 80%. Of the 19 patients tested in room air, five were stopped prior to 6 min of walking due to $S_{P,O_2}$ that reached 80%. Three patients with resting saturations >88% declined the additional test on 2 L of oxygen. Four of the five that were stopped prior to 6 min during the room air test completed 6 min on oxygen without desaturating to 80%. In the 16 patients tested on both room air and oxygen, walk distance increased from 271.2 m to 345.6 m when oxygen was administered during the test. The impact of supplemental oxygen and the reproducibility of the TWT were assessed in the subgroup that was tested both on and off oxygen. Walk distance increased by 27.5%, whilst walk velocity (17.8%) and change in saturation (19.3%) were less susceptible to the effect of supplemental oxygen. The intraclass correlation coefficient was 0.76 ($p=0.017$) for walk distance, 0.96 ($p<0.0001$) for walk

**TABLE 1** Baseline characteristics of the study population of patients with idiopathic pulmonary fibrosis

| Characteristics | |
|---|---|
| **Subjects n** | 28 |
| **Age yrs** | 62.7 (57–69) |
| **Male** | 19 (67.9) |
| **Smoking history** | 19 (67.9) |
| **Ethnic origin** | |
| Caucasian | 27 (96.4) |
| Other | 1 (3.6) |
| **FEV1 % pred** | 61.1 (45.3–70.8) |
| **FVC % pred** | 59.9 (42.5–71.5) |
| **TLC % pred** | 60.3 (45.5–67.5) |
| **$D_{L,CO}$ % pred** | 33.0 (23.0–43.3) |
| **$P_{a,O_2}$ mmHg** | 67.1 (56.5–80.0) |
| **$P_{a,CO_2}$ mmHg** | 40.2 (34.8–42.3) |
| **$P_{A-a,O_2}$ gradient mmHg** | 34.6 (21.6–45.4) |
| **Time since diagnosis yrs** | 3.1 (0.8–4.0) |
| **Duration of clinical symptoms yrs** | 4.3 (1.7–5.9) |
| **Method of diagnosis** | |
| SLB# | 14 (50) |
| Clinical and HRCT features (without SLB) | 14 (50) |

Data are presented as n, mean (interquartile range) and n (%). FEV1: forced expiratory volume in one second; % pred: % predicted; FVC: forced vital capacity; TLC: total lung capacity; $D_{L,CO}$: diffusing capacity for carbon monoxide, corrected to haemoglobin; $P_{a,O_2}$: arterial oxygen tension; $P_{a,CO_2}$: arterial carbon dioxide tension; $P_{A-a,O_2}$: alveolar–arterial oxygen tension; SLB: surgical lung biopsy; HRCT: high-resolution computed tomography. #: in addition to clinical and HRCT features. 1 kPa=0.133 mmHg.

velocity and 0.59 (p=0.047) for change in saturation, despite the addition of oxygen between the two tests.

### *Association of the timed walk test with pulmonary function*

To assess the relationship between the TWT and spirometry, lung volumes, $D_{L,CO}$ and arterial blood-gas parameters, the results of the TWT in room air or on 2 L of oxygen (according to the pre-specified criteria) were used. There were no correlations between the parameters of the TWT and the FVC, FEV1, total lung capacity and arterial carbon dioxide tension. There were strong correlations between $D_{L,CO}$, resting arterial oxygen tension ($P_{a,O_2}$) and $P_{A-a,O_2}$ difference, and end-exercise saturation, walk-distance and walk-velocity parameters of the TWT (table 2). Using a linear regression model, it was found that the relationship between $D_{L,CO}$ and the end-exercise saturation parameter of the TWT predicts a decrease of 11.8% pred $D_{L,CO}$ for each 5% decrement in end-exercise saturation (95% confidence interval (CI): 7.75–15.85), or a 36% difference in $D_{L,CO}$ relative to the mean value in this population (fig. 1a). Addition of the type of test (*i.e.* room air or oxygen), age, sex, FVC, time from diagnosis and time from onset of symptoms to the regression model did not alter this relationship. A linear regression model showed that the relationship between $D_{L,CO}$ and the walk-velocity parameter of the TWT predicts a decrease of 25.35% pred $D_{L,CO}$ for each 1 $m \cdot s^{-1}$ decrement in walk velocity (95% CI: 14.64–36.06; fig. 1b).

### *Association of the timed walk test with survival*

Patients were prospectively followed from enrolment for a median (range) of 5.4 yrs (4.3–6.2). Whilst 19 out of 28 (67.9%) patients died within 2 yrs from the time of the baseline TWT, 22 out of 28 (78.6%) died over the entire follow-up period at an average (range) of 1.2 yrs (0.2–3.0) from enrolment. During the study period, five patients underwent single-lung transplant at an average of 1.5 yrs (1.0–2.4) from enrolment and were censored in the analysis at the time of transplantation. In univariate Cox proportional-hazards models of survival, end-exercise saturation, change in saturation with exercise, walk distance and walk velocity were associated with mortality (table 3). The $D_{L,CO}$, which was highly correlated with parameters of the TWT, was also associated with survival. Addition of the use of supplemental oxygen during the TWT to the proportional-hazards model did not influence the estimate of relative hazard. Multivariate proportional-hazards models were created for parameters of the TWT (table 3). The addition of the use of supplemental oxygen, age, sex, FVC % pred and duration of symptoms did not appreciably alter the univariate estimates of the associations between parameters of the TWT and survival.

Kaplan–Meier survival analysis grouped according to tertiles of walk velocity showed that the median survival times were reduced according to the strata of walk velocity (fig. 2a; table 4; p=0.019, log rank test). Grouping according to tertiles of change in saturation with exercise demonstrated reduced survival according to strata by Kaplan–Meier survival analysis (fig. 2b; table 5; p=0.024, log rank test).

**TABLE 2** Associations between pulmonary function and parameters of the timed walk test

| Variable | $D_{L,CO}$ | | $P_{a,O_2}$ | | $P_{A-a,O_2}$ difference | |
|---|---|---|---|---|---|---|
| | r | p-value | r | p-value | r | p-value |
| **End-exercise $S_{P,O_2}$** | 0.80 | <0.001 | 0.57 | 0.001 | -0.57 | 0.005 |
| **Change in $S_{P,O_2}$ with exercise** | -0.63 | 0.001 | -0.33 | 0.129 | 0.33 | 0.129 |
| **Walk distance** | 0.77 | <0.001 | 0.67 | <0.001 | -0.67 | <0.001 |
| **Walk velocity** | 0.73 | <0.001 | 0.73 | <0.001 | -0.70 | <0.001 |

$D_{L,CO}$: diffusing capacity for carbon monoxide; $P_{a,O_2}$: arterial oxygen tension; $P_{A-a,O_2}$: alveolar–arterial oxygen tension; $S_{P,O_2}$: arterial oxygen saturation measured by pulse oximetry.

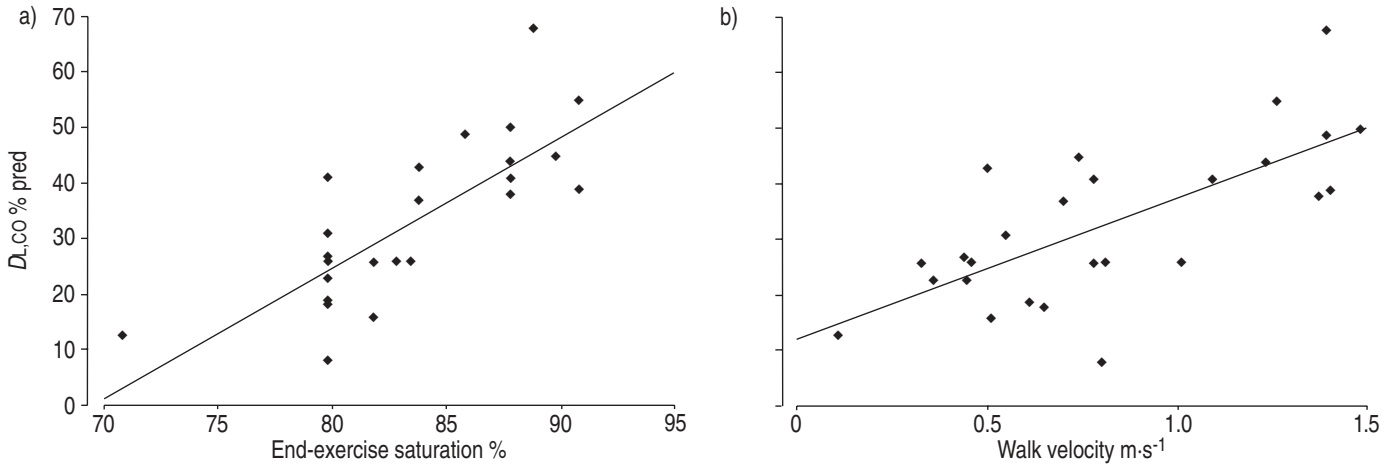


**FIGURE 1.** Relationships between diffusing capacity for carbon monoxide ($D_{L,CO}$) and a) end-exercise saturation and b) walk-velocity parameters of the timed walk test (TWT) in a population (n=26) of patients with advanced idiopathic pulmonary fibrosis. Least squares linear regression was used to describe the relationship between $D_{L,CO}$ and the TWT parameters (a) B=2.36, 95% confidence interval (CI): 1.55–3.17; b) B=25.35, 95% CI: 14.64–36.06).

To corroborate the findings of the proportional-hazards model, the associations between parameters of the TWT and 2-yr survival were assessed by logistic regression. According to an unadjusted logistic regression model, odds of death after 2 yrs were reduced with incremental improvements in end-exercise saturation, change in saturation with exercise, walk distance and walk velocity (table 6). $D_{L,CO}$ and resting $P_{a,O_2}$ were also associated with death after 2 yrs.

## DISCUSSION

IPF is a fatal disease with no known effective therapy. Clinicians need to provide accurate prognostic information to patients with IPF. In this study, the current authors describe a modified version of the 6MWT, the TWT, which is designed to capture information about the physiological limitations of patients with IPF with a broad range of disease severity. The TWT is a simple clinical tool that can be readily applied to clinical practice and incorporates information about haemoglobin saturation at rest and with exertion, characterises continuous walk velocity, and has a uniform approach to the use of supplemental oxygen during the test that is based on resting saturation. This is the first study to characterise the TWT in a well-defined population of patients with established IPF, showing that the TWT is associated with disease severity, gas exchange and long-term survival.

The 6MWT is widely used and provides important prognostic information in several chronic cardiopulmonary disease states [13–16]. The primary outcome measurement of the 6MWT is the distance walked during a period of 6 min, which may include periods of rest. In contrast, the TWT assesses the

**TABLE 3** Results of univariate and multivariate Cox proportional-hazards models relating parameters of the timed walk test and pulmonary function to mortality

| Variables | Univariate models | | Multivariate# models | |
|---|---|---|---|---|
| | Relative hazard (95% CI) | p-value | Relative hazard (95% CI) | p-value |
| **Resting room air $S_{P,O_2}$** | 0.93 (0.75–1.14) | 0.454 | 1.06 (0.83–1.37) | 0.637 |
| **End-exercise $S_{P,O_2}$ 2% units** | 0.73 (0.59–0.91) | 0.004 | 0.74 (0.55–1.00) | 0.051 |
| **Change in $S_{P,O_2}$ with exercise¶** | 0.80 (0.69–0.92) | 0.002 | 0.80 (0.67–0.96) | 0.014 |
| **Walk distance 30-m units** | 0.89 (0.81–0.97) | 0.010 | 0.91 (0.81–1.02) | 0.098 |
| **Walk velocity 0.1-m·s$^{-1}$ units** | 0.77 (0.65–0.91) | 0.002 | 0.76 (0.63–0.93) | 0.006 |
| **$D_{L,CO}$ % pred** | 0.93 (0.88–0.97) | 0.001 | 0.92 (0.87–0.98) | 0.005 |
| **FVC % pred+** | 1.00 (0.97–1.02) | 0.781 | 0.94 (0.97–1.02) | 0.646 |
| **Resting $P_{a,O_2}$ mmHg** | 0.97 (0.94–1.00) | 0.076 | 0.96 (0.91–1.01) | 0.101 |
| **Resting $P_{A-a,O_2}$ difference mmHg** | 1.01 (0.99–1.04) | 0.328 | 1.01 (0.97–1.05) | 0.672 |

CI: confidence interval; $S_{P,O_2}$: arterial oxygen saturation measured by pulse oximetry; $D_{L,CO}$: diffusing capacity for carbon monoxide; % pred: % predicted; FVC: forced vital capacity; $P_{a,O_2}$: arterial oxygen tension; $P_{A-a,O_2}$: alveolar–arterial oxygen tension. #: the multivariate model included age, sex, FVC % pred, time from the onset of symptoms and supplemental oxygen administration during the test; ¶: for consistency, change in saturation was entered as a negative change such that a lesser degree of desaturation would be associated with reduced mortality; +: the multivariate model excluded FVC as a covariate. 1 kPa=0.133 mmHg.

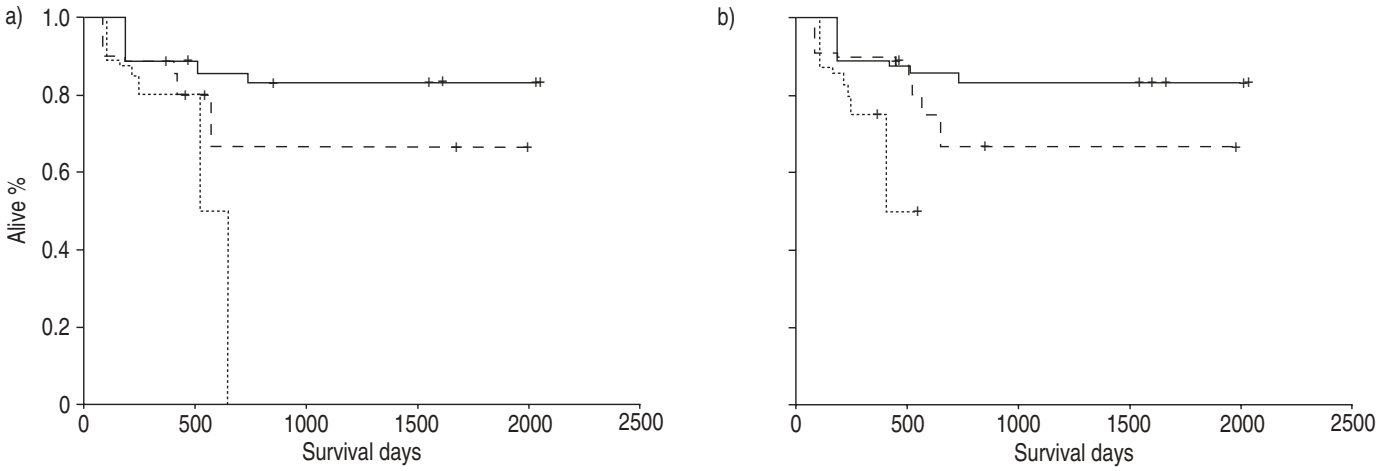


**FIGURE 2.** Kaplan–Meier survival curves according to the tertiles of a) walk velocity (——: highest tertile, median 1.38 m·s$^{-1}$; ----: middle tertile, median 0.76 m·s$^{-1}$; ·····: lowest tertile, median 0.45 m·s$^{-1}$; table 4) and b) change in saturation (——: lowest tertile, median 5; ----: middle tertile, median 10; ·····: highest tertile, median 14.5; table 5) parameters of the timed walk test. Survival curves were compared with the log rank statistic (a) p=0.019; b) p=0.024). +: censored.

**TABLE 4** Numbers at risk according to the tertiles of the walk-velocity parameter at different survival time points

| Number at risk | Survival days | | | | |
|---|---|---|---|---|---|
| | 0 | 500 | 1000 | 1500 | 2000 |
| **Highest tertile** | 9 | 7 | 4 | 4 | 2 |
| **Middle tertile** | 10 | 4 | 2 | 2 | 1 |
| **Lowest tertile** | 9 | 3 | 0 | 0 | 0 |

Data are presented as n.

**TABLE 5** Numbers at risk according to the tertiles of the change in saturation parameter at different survival time points

| Number at risk | Survival days | | | | |
|---|---|---|---|---|---|
| | 0 | 500 | 1000 | 1500 | 2000 |
| **Lowest tertile** | 9 | 7 | 5 | 5 | 5 |
| **Middle tertile** | 11 | 6 | 1 | 1 | 1 |
| **Highest tertile** | 8 | 1 | 0 | 0 | 0 |

Data are presented as n.

change in saturation and walk velocity during continuous exertion. The parameters of the TWT are designed to summarise important information about gas exchange and exercise performance, which relate to survival in IPF. For example, end-exercise $P_{a,O_2}$ during maximal exercise [7, 12] and submaximal steady-state exercise [12] are important measures of disease severity in IPF, leading to the hypothesis in this study that change in saturation during self-paced walking is a meaningful measure of disease status and outcome in IPF. This was also recently illustrated by LAMA *et al*. [17] who showed that, in a subgroup of patients with IPF without resting hypoxaemia, desaturation to 88% at any point during the 6MWT was associated with an increased hazard of death; however, the 6MWT distance was not associated with survival.

The TWT has specific criteria to end the test prior to 6 min, with the expectation that many patients with IPF are unable to complete 6 min of continuous exertion [17, 24]. A saturation of 80% was chosen as one of the stopping criteria in the TWT because of the potential for cardiac arrhythmias and inaccurate pulse oximetry tracings <80%. The data in the current study confirms that persons with IPF often demonstrate significant desaturation during 6 min of continuous walking, especially in

**TABLE 6** Results of univariate logistic regression models relating parameters of the timed walk test and pulmonary function to mortality

| Variables | Odds ratio (95% CI) | p-value |
|---|---|---|
| **Resting room air $S_{P,O_2}$** | 0.78 (0.56–1.11) | 0.169 |
| **End-exercise $S_{P,O_2}$ 2% units** | 0.45 (0.26–0.81) | 0.007 |
| **Change in $S_{P,O_2}$ with exercise**$^{\#}$ | 0.67 (0.48–0.94) | 0.020 |
| **Walk distance 30-m units** | 0.80 (0.68–0.95) | 0.012 |
| **Walk velocity 0.1-m·s$^{-1}$ units** | 0.67 (0.50–0.90) | 0.007 |
| **$D_{L,CO}$ % pred** | 0.83 (0.72–0.96) | 0.010 |
| **FVC % pred** | 1.00 (0.96–1.04) | 0.996 |
| **Resting $P_{a,O_2}$ mmHg** | 0.90 (0.83–0.99 | 0.030 |
| **Resting $P_{A-a,O_2}$ difference mmHg** | 1.05 (0.99–1.11) | 0.143 |

CI: confidence interval; $S_{P,O_2}$: arterial oxygen saturation measured by pulse oximetry; $D_{L,CO}$: diffusing capacity for carbon monoxide; % pred: % predicted; FVC: forced vital capacity; $P_{a,O_2}$: arterial oxygen tension; $P_{A-a,O_2}$: alveolar–arterial oxygen tension. $^{\#}$: for consistency, change in saturation was entered as a negative change such that a lesser degree of desaturation would be associated with reduced mortality. 1 kPa=0.133 mmHg.

the absence of supplemental oxygen. The standardised approach to the use of supplemental oxygen enabled the assessment of patients with marked differences in disease severity. The walk-distance parameter of the TWT was more susceptible to the addition of supplemental oxygen than the change in saturation parameter in patients with IPF without resting hypoxaemia. It was found that the change in saturation parameter of the TWT had a better association with survival than the walk-distance parameter in this diverse group of patients with IPF.

Exercise performance is a measurement of functional status that is assessed by the walk velocity in the TWT. Hypoxaemia impairs exercise performance in ILD [18, 19], suggesting that correction of hypoxaemia is necessary to fully assess this parameter. By using a two-tiered test based on baseline saturation, it was possible to correct hypoxaemia, if necessary, and assess the change in saturation parameter within a safe range for each patient. The walk-velocity parameter of the TWT has been used previously in chronic obstructive pulmonary disease (COPD) as a measure of functional status [25], and was a highly repeatable measure in the current study. The reproducibility of the walk-distance parameter of the TWT was similar to the reproducibility of 6MWT distance in COPD [26] and heart failure [27], and the walk-velocity parameter was highly reproducible, despite the addition of oxygen between the two tests in those patients without resting hypoxaemia.

The TWT is a clinically relevant, objective measure of disease severity in IPF. The $D_{L,CO}$, $P_{a,O_2}$ and $P_{A-a,O_2}$ difference, which are strongly associated with the walk velocity and end-exercise saturation in this study, reflect the severity of parenchymal abnormalities in IPF and have consistently been associated with clinically important endpoints [7, 8, 12, 28–31]. There was no clear association between the TWT and lung volumes in this study. However, lung volumes are inconsistently associated with survival and other outcome measures in IPF [2, 4], and changes in lung volumes are insensitive to the effect of treatment in clinical trials [10, 32].

Survival is a key outcome measure in IPF. This study demonstrates a strong relationship between a number of parameters of the TWT and survival in persons with IPF. The associations between parameters of the TWT and survival were shown using a proportional-hazard model and corroborated by logistic regression analysis of 2-yr survival. Due to the modest sample size, the current authors were unable to identify additional factors that might alter the associations between parameters of the TWT and mortality. Future studies in larger numbers of patients may be able to adjust for factors, such as sex and age, to refine the relationship between parameters of the TWT and survival. Since the parameters of the TWT are highly interdependent, it is not possible to state which parameter is most predictive. Similar to other recent studies, $D_{L,CO}$ was also associated with survival to a greater degree than lung volumes [33]. Longitudinal changes in measurements of resting physiological variables (composite index, FVC, $D_{L,CO}$) have been demonstrated to predict survival in IPF [34–36]. In the current study, the survival in the patient population was predicted by the TWT performed at the baseline visit itself. Additional advantages of the TWT over the $D_{L,CO}$ are that it can be conducted in an ambulatory setting and does not involve a breath-holding manoeuvre required for the $D_{L,CO}$, which may not be tolerated by some patients with advanced IPF.

This study has a few potential limitations, as follows. 1) The study population consisted of a small number of patients with IPF who had progressed despite conventional therapy. 2) The study was conducted at a single tertiary referral centre with expertise in the management of IPF. 3) The TWT was conducted by a single respiratory therapist. 4) The TWT was not conducted at the time of initial diagnosis and was not serially performed during follow-up. 5) The TWT was not compared with other functional measurements, such as the 6MWT or formal cardiopulmonary exercise test. 6) The treatment regimen subsequent to the TWT was not controlled for in the analysis. Acknowledging that there is no known effective therapy to date, individual therapies are unlikely to have confounded the relationship between the TWT and survival.

In summary, the timed walk test is a clinical tool that can be performed in the ambulatory setting and relates to important aspects of disease severity and long-term outcome in idiopathic pulmonary fibrosis. This simple functional measurement may have a role in the clinical evaluation of persons with idiopathic pulmonary fibrosis, and may serve as a reliable outcome measure to assess treatment response, guide timing of lung transplantation and predict long-term survival in idiopathic pulmonary fibrosis. Future studies comparing the timed walk test with the 6-min walk test and/or other exercise tests with continuous measurements of arterial oxygen saturation measured by pulse oximetry in patients with idiopathic pulmonary fibrosis are indicated to validate the findings of this study in a larger population.

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