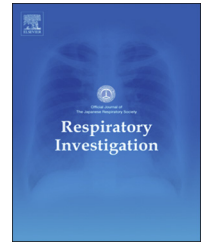




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## Original article

# Physical activity in daily life in patients with idiopathic pulmonary fibrosis



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## ABSTRACT

**Background:** Idiopathic pulmonary fibrosis (IPF) is characterized by progressive impairment of lung function and degradation of daily activity; however, this degradation has not been adequately elucidated. The objective of this study was to measure the physical activity of patients with IPF to determine its relationships with physiological parameters and survival rate. **Methods:** In total, 31 patients with IPF and 20 age-matched healthy participants were enrolled in this study. Physical activity was assessed using a physical activity monitor. The relationships among physical activity, physiological data, questionnaire-based patient-centered data, and survival were examined.

**Results:** Physical activity, expressed as daily activity energy expenditure (AEE), was significantly lower, and the percentage of sedentary time was significantly longer in patients with IPF than in healthy participants. Moreover, AEE was moderately correlated with body-mass index, forced vital capacity, diffusing capacity of carbon monoxide, and partial arterial pressure of oxygen. Relatively strong correlation was also observed between AEE and the 6-min walk distance, but not with daily dyspnea, depression, and health-related quality of life scores. Prognostic analysis indicated that daily AEE was a significant predictor of survival.

**Conclusions:** Patients with IPF were significantly inactive compared with age-matched healthy participants. In patients with more impaired physiological functions, the lower the physical activity was, the more was the sedentary time increased. Furthermore, lower daily physical activity resulted in significantly worse survival.

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Abbreviations: AEE, activity energy expenditure; BDI, Baseline Dyspnea Index; BMI, body mass index; COPD, chronic obstructive pulmonary disease; DLco, diffusing capacity of carbon monoxide; FEV<sub>1</sub>, forced expiratory flow in 1 s; fIIP, fibrotic idiopathic interstitial pneumonia; FVC, forced vital capacity; HADS, Hospital Anxiety and Depression Scale; IPF, idiopathic pulmonary fibrosis; PaCO<sub>2</sub>, partial arterial pressure of carbon dioxide; PaO<sub>2</sub>, partial arterial pressure of oxygen; SD, standard deviation; SGRQ, St. George's Respiratory Questionnaire; SpO<sub>2</sub>, transcutaneous oxygen saturation; 6MWD, 6-min walk distance; 6MWT, 6-min walk test

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## 1. Introduction

Idiopathic pulmonary fibrosis (IPF) is a debilitating disease that is characterized by progressive impairment in lung function and degradation of daily activity. Lung function, such as forced vital capacity (FVC), is now recognized as one of the important outcomes in clinical trials and cohort studies of IPF, because it significantly predicts survival [1]. Exercise capacity, such as a 6-min walk distance (6MWD) and maximal oxygen consumption measured by a cardiopulmonary exercise test, is decreased in IPF and is considered a significant predictor of survival [2–4]. However, the actual daily life physical activity in patients with IPF has not been adequately elucidated.

Recently, physical activity has been of focal interest in chronic obstructive pulmonary disease (COPD) [5]. Patients with COPD have reduced physical activity, which is not completely reflected by the disease severity when determined via the lung function [6,7]. More importantly, physical activity is reportedly a stronger predictor of survival than is forced expiratory volume in 1 sec (FEV<sub>1</sub>) and exercise capacity assessed by a 6-min walk test (6MWT) [8].

The question remains as to whether the reduction in physical activity due to IPF is similar to that in COPD and is associated with the survival rate. To address this, patients with IPF and age-matched healthy participants were prospectively recruited, and physical activity was measured to determine its relationship with physiological parameters and survival rate.

## 2. Patients and methods

### 2.1. Study population and design

This study was a prospective, controlled, observational study. A total of 31 patients with a diagnosis of IPF were prospectively recruited from outpatient settings in our university hospital (Kindai University Hospital, Osakasayama, Osaka, Japan) and represented the IPF group. The diagnosis of IPF was in accordance with the criteria set forth by the American Thoracic Society (ATS), European Respiratory Society, Japanese Respiratory Society, and Latin American Thoracic Association [9]. Patients were excluded if an infection or acute worsening of the disease had occurred within 3 months or if they had unstable comorbid illnesses. Further excluded were patients who could not undertake a pulmonary function test and a 6MWT, patients who were on any anti-inflammatory or antifibrotic therapy, and patients who were receiving long-term oxygen therapy. Eligible patients were evaluated for their physical activity and were followed-up to record mortality.

In addition, 20 age-matched healthy participants without lung disease were included in the control group. Their physical activities were also evaluated to enable a comparison with the eligible patients with IPF.

Written informed consent was obtained from all study participants. The study protocol was approved by the ethics

committee of Kindai University, Faculty of Medicine on December 13, 2010 (No. 22–49).

### 2.2. Measurement of physical activity

Patients and study participants were equipped with an Actical<sup>®</sup> physical activity monitor (Mini Mitter Co., Inc., Respironics, Inc, OR, USA). The Actical activity monitor is an accelerometer that senses motion in all directions. It is water resistant, lightweight (17 g), small (2.8 × 2.7 × 1.0 cm<sup>3</sup>), and has a data storage capacity of 64,800 data points that will saturate after 44 days of measurement using 1-min recording intervals. The monitors are initialized and downloaded using a serial port computer interface. The device measures the activity energy expenditure (AEE), which is defined as the relative energy expenditure to perform a task above resting metabolism and includes steps taken per day. Caloric expenditure was approximated for the time spent at four physical activity intensities: sedentary; light, ~0.031 kcal/min/kg; moderate, ~0.083 kcal/min/kg; and vigorous, ~0.083 kcal/min/kg. The accuracy of the Actical monitor for predicting AEE and the time spent at each activity intensity has been validated [10]. Participants were instructed to wear the monitoring device on their hip, using a strap, continuously for 7 consecutive days, except while bathing and sleeping. The AEE and time spent at each activity intensity were calculated based on the average daily value.

### 2.3. Pulmonary function tests

All study participants underwent spirometry (CHEST AC-55V; Chest, Tokyo, Japan), according to the method described in the guidelines of the ATS [11]. Single-breath diffusing capacity of the lung for carbon monoxide (DL<sub>CO</sub>) was also measured (CHEST AC-55V; Chest, Tokyo, Japan) [12]. The values of the forced vital capacity (FVC) and DL<sub>CO</sub> were related to the percentage of the predicted values [13,14].

### 2.4. The 6-min walk test

The 6MWT was conducted in all participants according to the ATS statement [15]. Briefly, all patients were tested under standardized conditions by trained physicians. After the baseline blood pressure, heart rate, and oxygen saturation were measured, patients were asked to walk as far as possible in 6 min. The total distance walked, as well as their heart rate and oxygen saturation immediately after the test, were recorded. Patients were also asked to rate their dyspnea at the end of the test using the modified Borg scale. Briefly, patients selected a number from 0 to 10, with 0 representing no dyspnea and 10 representing the maximal sustainable dyspnea [16].

### 2.5. Assessments of dyspnea in daily living, anxiety, depression, and health-related quality of life

The severity of dyspnea in daily living was assessed using the Baseline Dyspnea Index (BDI) [17], which recognizes three grades for each of the following categories: functional impairment, magnitude of the task, and magnitude of the effort.

The sum of the three categories was calculated as the BDI score. Permission for the use of the BDI was obtained from the Mapi Research Trust, Lyon, France.

Anxiety and depression were assessed using the Hospital Anxiety and Depression Scale (HADS) [18]. The HADS consists of two subscales for anxiety and depression, and a score  $\geq 8$  out of a possible score ranging from 0 to 21 is indicative of clinically relevant symptoms.

Health-related quality of life (HRQL) was assessed using St. George's Respiratory Questionnaire (SGRQ) [19], which provides three component scores representing symptoms, activity, and impacts, and a total score. The three component scores and the total score are assessed on a 100-point scale, with a higher score corresponding to a poorer HRQL. Permission for the use of the SGRQ was obtained from a representative of Dr. Koichi Nishimura (Obu, Aichi, Japan).

### 2.6. Assessment of survival

The survival rate of the patients was assessed up until November 20, 2016. The deaths among those patients who had been visiting our hospital for regular check-ups were identified by reviewing the hospital records. For patients who had moved to another hospital, we sought to obtain the survival status via a telephone interview conducted either directly with the patient when possible or through their family members. If the patient was deceased, we endeavored to obtain the date of death. The survival time was calculated as the period from the date of the study enrolment until the date of death. If a patient was still alive, the survival time was calculated as the period from the date of study enrolment to the last day when the patient was confirmed alive based on hospital records or a telephone interview; however, patients were treated as censored cases in the analysis.

### 2.7. Statistical analysis

Quantitative variables were expressed as the mean  $\pm$  standard deviation (SD), while qualitative variables were presented as frequencies. Comparisons of the quantitative variables between patients with IPF and healthy participants were performed using the Mann-Whitney *U* test. Spearman's correlation coefficients ( $\rho$ ) were determined to examine the degree of correlation among physical activity variables and other variables (e.g., physiological). A chi-square test was performed to compare the proportions between the two groups.

Univariate Cox proportional-hazard models were used to examine the association of selected variables with survival. To compare the relative risks among the predictors, we divided all continuous variables by a 0.5 SD to reveal standardized units. Stepwise multivariate Cox proportional regression analysis was performed using variables of significance from the univariate analysis. Kaplan-Meier survival estimates were compared using the log-rank test for the patient's daily AEE. All tests were performed at a significance level of  $p < 0.05$ . Analyses were performed using the PASW statistical package, version 18 (SPSS Japan Inc., Tokyo, Japan).

## 3. Results

Thirty-one patients with IPF were identified as eligible between March 2011 and February 2013 and were included in the study. The mean age of the patients was  $72.3 \pm 5.2$  years, and 23 (74%) of the 31 patients were male. The baseline clinical and physiological characteristics of the patients are summarized in Table 1. The mean age of the healthy participants was  $72.7 \pm 5.3$  years, and 4 (20%) of them were male. There was no significant difference in age

**Table 1 – Baseline demographic and disease characteristics of patients with IPF and healthy participants (control).**

Variables <sup>a</sup>	IPF <sup>b</sup>	Control
Patients/participants, n	31	20
Age, yrs	$72.3 \pm 5.2$	$72.7 \pm 5.3$
Gender, n		
Male	23	4
Female	8	16 <sup>**</sup>
Height, cm	$159.3 \pm 7.9$	$154.0 \pm 8.4^*$
Body weight, kg	$58.8 \pm 9.7$	$51.1 \pm 7.7^{**}$
BMI, kg/m <sup>2</sup>	$23.1 \pm 3.1$	$21.6 \pm 3.4^*$
Pulmonary function testing		
FVC, L	$2.31 \pm 0.73$	–
FVC, % pred	$73.8 \pm 18.3$	–
DLco, mL min <sup>-1</sup> mmHg <sup>-1</sup>	$10.0 \pm 3.3$	–
DLco, % pred	$61.0 \pm 16.7$	–
Arterial blood gas values		
PaO <sub>2</sub> , mmHg	$75.5 \pm 8.4$	–
6-min walk test		
Walk distance, m	$410 \pm 78$	–
Lowest SpO <sub>2</sub> , %	$84.3 \pm 7.8$	–
Borg scale	$4.9 \pm 2.0$	–
BDI	$7.7 \pm 2.0$	–
SGRQ		
Symptoms	$50.0 \pm 24.4$	–
Activity	$50.2 \pm 25.0$	–
Impacts	$32.2 \pm 20.6$	–
Total	$40.9 \pm 20.6$	–
HADS		
Anxiety	$6.2 \pm 3.1$	–
Depression	$6.0 \pm 2.7$	–

BDI, Baseline Dyspnea Index; BMI, body mass index; FVC, forced vital capacity; DLco, diffusion capacity of carbon monoxide; HADS, Hospital Anxiety and Depression Scale; IPF, idiopathic pulmonary fibrosis; PaO<sub>2</sub>, arterial partial pressure of oxygen; Pred, predicted; SGRQ, St. George's Respiratory Questionnaire; SpO<sub>2</sub>, arterial oxygen saturation measured by pulse oximetry.

<sup>a</sup> Continuous variables are expressed as mean values  $\pm$  standard deviations.

<sup>b</sup> In IPF group:  $n = 28$  for DLco and  $n = 28$  for %DLco.

\*  $p < 0.05$ .

\*\*  $p < 0.001$  compared with patients with IPF.

**Table 2 – Physical activity in patients with IPF and healthy participants (control).**

Activity variables	IPF	Control	p-value
Patients/participants, n	31	20	
Daily steps, n	2728 ± 2475	5953 ± 3578	0.0005
AEE, kcal/day	133 ± 127	201 ± 111	0.01
Sedentary, % of day	93.2 ± 5.3	87.2 ± 7.0	0.001
Light activity, % of day	5.4 ± 3.9	10.1 ± 6.4	0.005
Moderate activity, % of day	1.3 ± 1.9	2.5 ± 2.5	0.07
Vigorous activity, % of day	0 ± 0	0.01 ± 0.04	0.07

AEE, activity energy expenditure; IPF, idiopathic pulmonary fibrosis.

Light activity, ~0.031 kcal/min/kg; moderate activity, ~0.083 kcal/min/kg; and vigorous activity, ~0.083 kcal/min/kg.

between patients and healthy participants ( $p = 0.80$ ), but the proportion of males, height, body weight, and body mass index (BMI) was significantly higher in the patient group than in the control group.

As shown in Table 2, the patients took significantly fewer steps per day than the healthy participants. Physical activity per day, expressed as AEE, was also significantly lower in patients than in the control group. The patients remained sedentary significantly longer and showed significantly reduced participation in light activity than did the control group. Participation in moderate and vigorous activities was too short for both groups and no significant difference could be determined.

For the patients with IPF, the correlation of physical activity with other variables is shown in Table 3. The number of steps per day was moderately correlated with FVC, DLco, arterial partial pressure of oxygen ( $\text{PaO}_2$ ), and the 6MWD ( $\rho$ , 0.41–0.53). The value of AEE per day was moderately correlated with BMI, FVC, DLco, and  $\text{PaO}_2$  ( $\rho$ , 0.42 to 0.56), and relatively strongly correlated with the 6MWD ( $\rho = 0.71$ ). The percentage of sedentary time was moderately correlated with age ( $\rho = 0.39$ ), and was negatively correlated with BMI, FVC, DLco,  $\text{PaO}_2$ , and the 6MWD ( $\rho$ , –0.68 to –0.37). No significant correlations were noted between the physical activity variables and the BDI, SGRQ, and HADS scores.

The mean observation period was  $1007 \pm 531$  days. Among the 31 patients with IPF, 23 (74.2%) died during the study. The results of the univariate Cox proportional hazard analysis are shown in Table 4. The variables significantly associated with survival were as follows: higher FVC (hazard ratio [HR] 0.45, 95% confidence interval [CI] 0.22–0.93;  $p = 0.03$ ), longer 6MWD (HR 0.99, 95% CI 0.98–0.99;  $p = 0.02$ ), higher AEE (HR 0.99, 95% CI 0.98–0.99;  $p = 0.005$ ), and longer time spent performing light activity (HR 0.86, 95% CI 0.76–0.97;  $p = 0.01$ ). However, a longer sedentary time was revealed to be significantly associated with worse survival (HR 1.12, 95% CI 1.02–1.23;  $p = 0.01$ ). The highest relative risk of death was observed for a standardized decrease in AEE (189%), followed by 6MWD (149%) (Fig. 1). In a stepwise multivariate analysis including the percentage of predictive FVC (%FVC), 6MWD, BMI, depression score, and AEE per day, only AEE per day (HR 0.99, 95% CI 0.98–0.99;  $p = 0.005$ ) was significantly associated with survival. The DLco was not included in either analysis because data were lacking. In addition, the percentage of

**Table 3 – Correlation between physiological and clinical variables with physical activity and time spent sedentary.**

Variables	Steps		AEE		% of sedentary time	
	$\rho$	p-value	$\rho$	p-value	$\rho$	p-value
Age	–0.04	0.73	–0.20	0.15	0.39	0.03
BMI	0.03	0.79	0.54	0.002	–0.44	0.01
FVC	0.41	0.01	0.56	0.001	–0.48	0.007
% pred FVC	0.35	0.05	0.53	0.003	–0.51	0.005
DLco	0.49	0.01	0.61	0.001	–0.48	0.01
% pred DLco	0.37	0.05	0.45	0.01	–0.37	0.05
$\text{PaO}_2$	0.47	0.009	0.42	0.02	–0.37	0.04
6-min walk test						
Walk distance	0.53	0.003	0.71	< 0.0001	–0.68	0.0002
Lowest $\text{SpO}_2$	0.21	0.23	0.31	0.08	–0.23	0.20
Borg scale	–0.09	0.61	–0.31	0.08	0.25	0.16
BDI	0.13	0.74	0.22	0.22	–0.18	0.31
SGRQ						
Symptoms	0.06	0.74	0.09	0.59	–0.21	0.23
Activity	–0.30	0.09	–0.03	0.86	0.03	0.85
Impacts	–0.20	0.25	0.03	0.86	–0.07	0.68
Total	–0.22	0.21	0.02	0.87	–0.08	0.64
HADS						
Anxiety	0.02	0.90	–0.03	0.84	0.02	0.87
Depression	0.004	0.98	–0.22	0.21	0.20	0.25

The  $n = 31$ , except for DLco ( $n = 28$ ) and %DLco ( $n = 28$ ).

The walk distance and lowest  $\text{SpO}_2$  are variables of the 6-min walk test.

AEE, activity energy expenditure; BMI, body mass index; FVC, forced vital capacity; DLco, diffusion capacity of carbon monoxide; HADS, Hospital anxiety and depression scale;  $\text{PaO}_2$ , arterial partial pressure of oxygen; Pred, predicted; SGRQ, St. George's Respiratory Questionnaire;  $\text{SpO}_2$ , arterial oxygen saturation measured by pulse oximetry.

sedentary time and the percentage of time spent participating in light activity were not included because of the significant negative and positive correlation with AEE, respectively. When the absolute FVC value was included in the analysis instead of %FVC, the result did not change. When adjusted with age, sex, and %FVC, which had been previously reported to be significant prognostic factors [20], AEE per day was still significantly associated with survival (HR 0.99, 95% CI 0.98–0.99;  $p = 0.009$ ). Kaplan-Meier survival curves based on AEE are shown in Fig. 2. The median survival estimates for patients with higher and lower AEEs than the median value of 87.67 kcal/day were 1754 days and 579 days, respectively. Patients with higher physical activity showed significantly better survival compared with those with lower physical activity (log-rank,  $p = 0.001$ ).

#### 4. Discussion

The results of the present study demonstrated that physical activity, expressed as steps taken and AEE, was significantly



**Table 4 – Results of univariate Cox proportional-hazard model.**

Variables	Hazard ratio	95% CI	p-value
Age, years	1.01	0.94–1.10	0.74
Gender			
Female	1.70	0.69–4.24	0.25
BMI	0.88	0.76–1.00	0.06
FVC	0.45	0.22–0.93	0.03
% pred FVC	0.98	0.96–1.01	0.15
DLco	0.86	0.74–1.00	0.05
% pred DLco	0.98	0.96–1.01	0.28
PaO <sub>2</sub>	0.96	0.90–1.01	0.13
6-min walk test			
Walk distance	0.99	0.98–0.99	0.01
Lowest SpO <sub>2</sub>	0.97	0.91–1.02	0.22
Borg scale	1.21	0.97–1.50	0.10
BDI	0.82	0.65–1.04	0.10
SGRQ			
Symptoms	1.01	0.99–1.02	0.61
Activity	1.00	0.99–1.02	0.89
Impacts	1.00	0.98–1.02	0.91
Total	1.00	0.98–1.02	0.94
HADS			
Anxiety	1.03	0.90–1.18	0.68
Depression	1.15	1.00–1.33	0.06
Daily step number	1.00	1.00–1.00	0.14
AEE	0.99	0.98–0.99	0.005
% of day sedentary	1.12	1.02–1.23	0.01
% of day performing light activity	0.86	0.76–0.97	0.01
% of day performing moderate activity	0.64	0.40–1.01	0.06

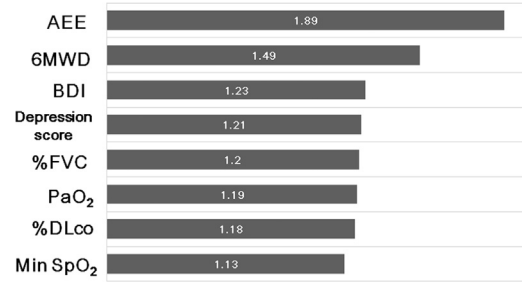
The  $n = 31$ , except for DLco ( $n = 28$ ).

Hazard ratios for female sex are in relation to male sex.

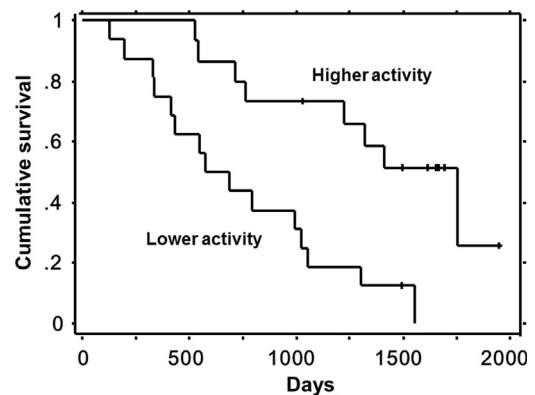
The walk distance and lowest SpO<sub>2</sub> are variables of the 6-min walk test.

AEE, activity energy expenditure; BMI, body mass index; CI, confidence interval; FVC, forced vital capacity; DLco, diffusion capacity of carbon monoxide; HADS, Hospital anxiety and depression scale; PaO<sub>2</sub>, arterial partial pressure of oxygen; Pred, predicted; SGRQ, St. George's Respiratory Questionnaire; SpO<sub>2</sub>, arterial oxygen saturation measured by pulse oximetry.

reduced in patients with IPF compared with healthy age-matched participants. Moreover, the patients remained sedentary for a significantly longer time and exhibited a reduced participation in light activity than did the healthy participants. Although the AEE and steps walked were moderately correlated with physiological variables such as FVC and DLco, AEE was more strongly correlated than were the steps walked. In the univariate survival analysis, the FVC, 6MWD, depression score, AEE, percentage of sedentary time, and percentage of time performing light activity were



**Fig. 1 – Comparison of the relative risk of death associated with physical activity and other established predictors of mortality. The relative risk was calculated for each 0.5 SD decrease except depression score which was for 0.5 SD increase. AEE, activity energy expenditure; BDI, Baseline Dyspnea Index; %DLco, percentage of predicted disusing capacity for carbon monoxide; %FVC, percentage of predicted forced vital capacity; Min SpO<sub>2</sub>, minimum arterial oxygen saturation measured by pulse oximetry at 6-min walk test; PaO<sub>2</sub>, arterial partial pressure of oxygen; 6MWD, 6-min walk distance.**



**Fig. 2 – Kaplan-Meier survival curves based on the activity energy expenditure (AEE) ( $p = 0.001$ ) (higher activity: AEE > 87.67 kcal/day; lower activity: AEE ≤ 87.67 kcal/day). There are 15 and 16 patients in the higher and lower activity groups, respectively. The median survival estimates for patients with higher and lower AEEs than the median value of 87.67 kcal/day are 1,754 days and 579 days, respectively. Survival curves were compared with log-rank statistics. +: censored.**

significantly associated with survival, but not the number of steps per day. In the stepwise multivariate survival analysis, only AEE was shown to be significantly prognostic.

Evaluating physical activity in daily life is a more recent focal point of interest among COPD researchers [5]. Although physical activity has been reported to be moderately correlated to exercise capacity when evaluated by either the 6MWT or a cardio pulmonary exercise test, only a weak-to-moderate association has been demonstrated between physical activity and FEV<sub>1</sub> in COPD [5]. It was also reported that

the 6MWD could not identify reliably the physically inactive patients with COPD [21]. More importantly, it was determined in several previous studies that physical activity is the most significant indicator of survival [6,8,22].

Currently, the data reported on patients with IPF are limited. Wallaert et al. [23] reported a significantly reduced physical activity in patients with fibrotic idiopathic interstitial pneumonia (fIIP) compared with healthy participants. Furthermore, they reported a significant correlation between physical activity and survival in univariate analysis, but not in a multivariate model [23]. This study assessed both steps walked and energy expenditure, steps walked per day was considered to discriminate better between patients and healthy participants. In our present study, patients with IPF were exclusively recruited.

It is important to focus solely on patients with IPF when evaluating survival, because both mortality and response to therapy are different between patients with IPF and other patients with fIIP [24]. Nakayama et al. [25] examined physical activity exclusively in patients with IPF and reported that dyspnea assessed using the modified Medical Research Council, 6MWD, extent of fibrosis on chest high-resolution computed tomography, and serum Krebs von den Lungen-6 levels were significant correlates [25]. In recent reports, it was demonstrated that the level of physical activity assessed by simple questionnaires was associated with survival [26,27]. However, to our knowledge, the present study is the first to evaluate the actual physical activity and to demonstrate its prognostic significance exclusively in patients with IPF.

In the analysis for correlates, the steps walked and AEE were reduced and the percentage of sedentary time increased as the pulmonary function deteriorated. It indicated that patients became increasingly inactive as their condition worsened. Interestingly, our results indicated that the BDI, SGRQ score, and HADS score did not correlate with variables of physical activity. In patients with IPF, it was shown that physical activity was associated with the actual disease severity, but not with their symptoms and HRQL.

It was surprising that patients with IPF spent most of their time sedentary. Furthermore, it was also important that AEE, but not the steps walked, significantly predicted the patient survival. Given that this finding is similar to previous findings in patients with COPD [8], our results indicated that evaluating physical activity using an accelerometer should be considered when assessing physical activity in chronic respiratory diseases. Focusing on the daily behavior of patients should be considered in clinical practice with respect to IPF in the immediate future. The results of the present study may cause a paradigm shift in both the care and treatment of patients with IPF, because physical activity has never been of focal interest.

If the physical activity level in daily life is improved and/or the percentage of time spent sedentary per day is shortened in patients with IPF, there may be a strong possibility that survival can be prolonged. Exercise capacity in patients with IPF reportedly improves with pulmonary rehabilitation, which consists of exercise training [28–30]. Whether or not improving the exercise capacity leads to increased physical activity will need to be further investigated in future studies, although such claim has been disputed in COPD [5]. It is

reasonable to hypothesize that improving the exercise capacity of patients with IPF, and providing them with counseling and social support to increase their contact with the rest of the society, is much needed. It is also crucial to minimize the loss of physical activity experienced by these patients during the course of their disease. Whether behavioral interventions initiated at the early stages of IPF can be efficacious are possibilities that warrant further investigations.

The limitations of this study included the small number of participating patients. Indeed, the fact that the %FVC, the lowest SpO<sub>2</sub>, the 6MWT, and dyspnea in daily life have been recognized as valid predictors of survival [1,31–33], but were not selected as prognostic factors in this study, might be attributed to the small number of patients. It might also be possible that physical activity had a stronger impact on survival than FVC. In the future, collecting additional data from a larger number of patients from multiple institutes is warranted to confirm our findings. Second, the proportion of healthy female participants was high in the control group, and the average height, body weight, and BMI were lower in this group compared with the patient group. Had the proportion of healthy male participants been higher in the control arm, the AEE of this group would likely have increased. Consequently, the difference in physical activity between the two groups might have become more emphasized. Third, the results were not necessarily applicable to patients with severer condition, because patients who could not undergo a pulmonary function test and/or patients with supplemental oxygen were excluded from the study. Our results should be confirmed in further studies without these kinds of restrictions. Nevertheless, this study provided a robust rationale for future studies investigating physical activity in IPF.

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## 5. Conclusions

In summary, the present study demonstrated that physical activity was reduced and time spent sedentary was increased in patients with IPF. A lower daily physical activity was prognostic for a significantly worse survival in these patients.

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## Conflicts of interest

The authors have no conflicts of interest.

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