Physical activity is associated with disease severity in idiopathic pulmonary fibrosis: a cross-sectional study

Jyotika Devi Prasad (j.prasad@alfred.org.au)
Alfred Health https://orcid.org/0000-0002-7903-7847
Anne E Holland
Monash University
Ian N Glaspole
Monash University
Glen P Westall
Monash University

Research article

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Abstract

Background

Physical inactivity is associated with poor outcomes in patients with many chronic lung diseases, however little is known about physical activity in patients with idiopathic pulmonary fibrosis (IPF). Our aim was to describe daily physical activity (DPA) in patients with a confirmed diagnosis of IPF and analyse its associations with traditional markers of disease severity and quality of life.

Methods

Fifty-nine patients with IPF had DPA parameters and sedentary time assessed with the Sensewear armband for seven consecutive days. Participants completed the Hospital Anxiety and Depression scale (HADS), St Georges Respiratory Questionnaire (SGRQ) and Leicester Cough Questionnaire (LCQ). Data on current markers of disease severity; forced vital capacity (FVC), carbon monoxide diffusion capacity (DLCO) and 6-minute walk test (6MWT) as well as prognostic markers; composite physiologic index (CPI) and gender age and physiology (GAP) was collected.

Results

Patients had a median daily step count of 3957 (300–7614), mean daily moderate to vigorous (MV) physical activity duration of 8.6 minutes (-13.1 to 30.3) and mean total daily sedentary time of 1234.6 minutes (± 122.8). Patients with early stages of IPF according to GAP stage had significantly higher daily step count than those with more severe disease ($p < 0.003$). Age, BMI and DLCO accounted for 54% variability in physical activity duration. The 6-minute walk distance and DLCO accounted for 44% variability in daily step count. Patient reported outcomes had weak association with daily step count and MV physical activity duration.

Conclusion

In IPF, increasing disease severity is associated with reduced DPA. DPA may be a meaningful outcome for future trials of therapies designed to enhance patient functioning and wellbeing.

Trial Registration: please note that a request has been made for retrospective registration with the Australian New Zealand Clinical Trial Registry with the request number being 381161. Due to holiday period closure, this is yet to be processed. I will supply this as soon as accepted.

Background

Idiopathic pulmonary fibrosis (IPF) is a chronic restrictive lung disease characterised by progressive dyspnoea and debilitating cough (1). The management of IPF is challenging due to its variable clinical evolution and the inability to accurately predict disease progression (2). Despite the emergence of novel antifibrotic therapy in the last decade, the prognosis remains poor with eventual functional decline and poor health-related quality of life (HRQOL) (3, 4). Whilst these new therapies have slowed decline in respiratory function, it has been more difficult to document improvements in clinically meaningful outcomes such as how a patient feels, functions or survives (5).

Currently, there is no validated direct measure of functional status in patients with IPF(6). A surrogate endpoint such as the six-minute walk distance (6MWD) is used to assess functional exercise capacity (7, 8) but does not fully capture how a patient carries out their daily activities away from the hospital setting. Current recommended markers of disease progression that have been used in pivotal interstitial lung disease (ILD) studies include forced vital capacity (FVC) and diffusing capacity for carbon monoxide (DLCO) (2). However, these are performed in a resting state at a single time point and may not accurately reflect functional capacity and HRQOL.

In chronic lung diseases such as chronic obstructive pulmonary disease (COPD), regular physical activity is associated with better quality of life and lower morbidity and mortality (9–11). In an observational study of patients with cystic fibrosis (CF), those who achieved general population targets for physical activity had better clinical outcomes such as reduced hospital days over a 12-month period (12). While evaluating physical activity levels, it is also important to examine sedentary behaviour, as prolonged periods of sedentary behaviour are independently associated with poor outcomes (13).

There is limited published literature on daily physical activity (DPA) in patients with IPF and the best tools for assessment of DPA. In a recent study, subjective (patient reported) measures of prolonged daily sitting time and shorter weekly walking time were associated with increased hospitalisations and mortality, although this was no longer significant in a multivariate analysis (14). Studies looking at objective measures of DPA and sedentary time in patients with ILD using wearable devices have shown reduced DPA levels (15–17) and elevated sedentary time (16, 18). However, the relationship between physical activity and clinical characteristics such as physiologic impairment and patient reported outcomes, remains inconclusive. Variations in how DPA is defined limit between-study comparisons, and little is known of the relationship between disease severity and physical activity as well as the impact of comorbidities which are commonly associated with IPF.

To understand the determinants and health related outcomes of physical activity in IPF, we need to improve our understanding of physical activity including intensity, frequency and duration. The objectives of this study were to; (1) describe DPA in patients with a confirmed diagnosis of IPF and (2) analyse its associations with current markers of disease progression, quality of life measures, prognostic markers and comorbidities.

Methods

Subjects

Patients with an Interstitial Lung Disease Multidisciplinary Meeting (ILD MDM) consensus diagnosis of IPF based on current international (2) and national guidelines (19) were approached at the ILD clinic at the Alfred Hospital for inclusion in the study. The study was granted ethical approval by the Alfred Health Office of Ethics and Research Governance (Project Reference: 107/15) and adheres to STROBE guidelines. Patients were excluded if unable to provide informed consent or if below the age of 18 years. Patients were recruited from May 2015 to March 2017.

Clinical Data

Patient demographic and health related information was collected from medical records. All participants underwent pulmonary function testing (PFT) and six-minute walk test (6MWT). Spirometry was performed according to ATS/ ERS criteria in an accredited laboratory and results of forced expiratory volume in one second (FEV_1), forced vital capacity (FVC), FEV_1/FVC ratio and diffusion capacity of carbon monoxide (DLCO) were recorded in standard units and percentage predicted values (20). Functional capacity was assessed with a 6MWT in accordance with ATS standards (21) . The six-minute walk distance (6MWD) and the baseline and minimum oxygen saturation (O_2Sat) and peak heart rate (HR) were recorded. Composite prognostic scores were calculated using gender, age and physiology (GAP) index and stage (22) and composite physiologic index (CPI) score (23). Participants completed three questionnaires: the St. George's Respiratory Questionnaire (SGRQ)(24), the Leicester Cough Questionnaire (LCQ) (25) and the Hospital Anxiety and Depression Score (HADS) (26).

Measurement of physical activity

All participants were requested to wear the SenseWear Armband ™ (SenseWear Pro; BodyMedia Inc., Pittsburgh, PA, USA (SAB)) version 6 on the triceps brachii of their non-dominant arm for 24 hours per day for seven consecutive days. The armband was only removed for activities with high risk of water damage to the SAB such as showering. The SAB is a lightweight, small metabolic monitor which estimates energy expenditure via a triaxial accelerometer and non-invasive physiologic measures such as heat flux, skin temperature and galvanic skin response(27). A valid measure was considered as at least 22 hours of data on at least 4-week days and one weekend day(28). Raw data from SAB were used to calculate total daily energy expenditure (TEE); active energy expenditure (AEE); physical activity duration (PAD), defined as, duration of activity at ≥ 1.5 metabolic equivalence of task (METs) and moderate to vigorous physical activity duration (MVPAD) defined as activity at ≥ 3 METs; total sedentary time (TST) defined as duration spent in activity between 0 to <1.5 METs; and steps per day (SPD). A Microsoft Excel™ macro was used to process raw data from the SAB to obtain physical activity variables.

Statistical Analysis

Data analysis was completed using IBM Statistical Package for Social Science (SPSS, Chicago, Ill, USA) version 22 or SAS version 9.4 (SAS Institute, Cary, NC, USA). Descriptive data are reported where appropriate as mean and standard deviation (normally distributed) or median and interquartile range and as percentages.

Patients were divided into groups based on GAP stage and one-way ANOVA was used to assess differences in clinical characteristics between groups. Univariable linear regression was undertaken to assess the relationship between current markers of disease severity, GAP index, CPI and patient reported outcomes with DPA parameters. Analysis of variance was used to determine relationship of daily steps and 6MWD with IPF stage. Independent t-tests were used to analyse the differences in 6MWD and daily steps in patients with no vs one or more comorbidity. Variables with a p value < 0.2 in the univariable linear regression were introduced into stepwise multiple linear regression model to identify variables independently associated with physical activity parameters and the predictive power of the model was assessed by the r^2 value. Prognostic score, that is, CPI was excluded from the multiple linear regression model for the physical activity parameters of daily step count and total sedentary time due to collinearity. A p value of <0.05 was considered significant.

Results

Participants

The study cohort consisted of 59 people with IPF. Fifty-six patients were included in the analysis. All participants wore SAB for one week, however three participants were unable to perform 6MWT and one did not complete all questionnaires. Demographic and baseline physiological data are in Table 1 and 2. Dyspnoea on exertion (92%) and cough (80%) were commonly reported. Comorbidities were common, and a significant proportion of patients were on antifibrotic therapy (67%) and oxygen therapy (39%). The mean FVC % predicted was 71% (±17) and mean DLCO % predicted was 46% (±17). The frequency of GAP stage was 45.8 % in stage I, 40.7 % in stage II and 13.6% in stage III. Mean 6MWT distance was 433m (±130) with median end 6MWT oxygen desaturation of 86% (75.5-96.5).

Daily Physical Activity

Average daily wear time was 23.6 (23.1-23.76) hours with mean of 6 days (4-7) of data captured per patient (Table 1). Participants showed low levels of physical activity, with average daily steps of 3957 (300-7614) and an average of only nine minutes per day in moderate to vigorous physical activity (13.1-30.3) (Table 3). Average physical activity duration was 188 minutes (±14), and the average total sedentary time was 1235 minutes (±123).

Determinants of daily physical activity: Univariate analysis

Univariate relationships between physical activity variables and patient characteristics are shown in Table 4. Overall, these relationships were weak to moderate. The most consistent relationships were seen between physical activity variables and 6MWD, DLCO % predicted and composite prognostic indices. Presence of comorbidities was significantly associated with daily step count (*Figure 1*).

Composite prognostic indices and daily physical activity: Univariate analysis

Composite prognostic indices as measured by GAP and CPI scores were associated with physical activity parameters but most strongly with steps per day. While patients in GAP stage I had 5340 (± 3348) steps per day with 23(± 25) minutes of daily high intensity activity duration, patients in stage III had 2533 (± 2166) steps per day with only 5 (± 6) minutes of daily high intensity activity duration (*Figure 2*). *Figure 3* shows a significant inverse relationship between CPI and steps per day and the CPI accounted for 25% of variability in steps per day. Patients with a CPI score of > 41 had mean steps per day of 3205 (± 2298) with 14 (± 23) minutes of daily high intensity activity duration, patients with CPI ≤ 41 had mean steps per day of 6494 (± 3476) (*Figure 4*) and daily high intensity activity duration of 30 (± 27) minutes.

Multiple Regression analysis

In the stepwise multiple regression, FVC % predicted and patient reported outcomes were not statistically significant predictors of any of the physical activity parameters. In separate regression analyses models, a combination of age, BMI, DLCO, 6MWD and IPF stage were the only statistically significant predictors of physical activity parameters (Table 5). Forty two percent of the daily step count variability was predicted by DLCO and 6MWD.

Discussion

This study was undertaken to provide a detailed description of daily physical activity (DPA) levels in patients with MDM-confirmed IPF and evaluate its association with conventionally used markers of IPF disease severity. We extended this analysis to report the association of DPA with several other relevant clinical and patient reported variables. The results confirmed our expectations that IPF patients have low levels of DPA and high sedentary time. Whilst disease severity (measured by DLCO) was an important determinant of DPA, other non-respiratory factors were also important, particularly age, BMI and functional exercise capacity.

Similar to previous studies (15–17), we found that daily step counts were markedly reduced compared to values that have been reported in healthy adults of a similar age(15).

In addition, we have shown that decreased DPA in patients with IPF is already present in early stages of physiologic impairment as defined by CPI, which has been identified as a more powerful prognostic marker of mortality then either lung function or alveolar arterial O2 gradient (23), and worsens as disease severity progresses, similar to patients with COPD (29). Troosters et al showed that patients with GOLD-stage II COPD had reduced DPA and this reduction worsened with increasing GOLD stage. A CPI score of > 41 has been demonstrated to have association with increased 3-year mortality(30). Our study demonstrated a significant reduction in steps walked per day in patients with a CPI score > 41 and between patient in GAP stage II and III compared with stage I. The modest association between 6MWD and DPA (Tables 4 and 5) further emphasises the need for direct assessment of daily functioning away from the hospital. The reduction in physical activity with increasing disease severity, without changes in total energy expenditure, highlights the need for improved understanding of contributors to energy expenditure and strategies to enhance physical activity in people with IPF.

Interestingly, despite FVC commonly being used in the pivotal IPF antifibrotic studies, it did not correlate well with DPA, with DLCO and 6MWD being better independent predictors of various DPA parameters. The association between spirometry and DPA has not been demonstrated in all IPF studies (15–17). While demonstrating a significant correlation with FVC % predicted and DPA on simple linear regression, this relationship was no longer significant in the multiple regression model. The 6MWD and DLCO % predicted were the only independent predictors of steps per day accounting for 42% of variability which is similar to results from Wallaert et al(15).

Overall, patients with IPF, irrespective of disease severity, were not spending significant periods performing higher intensity activity. Current American College of Sports Medicine (ACSM) recommendation for endurance exercise for healthy older adults is at least 30 to 60 minutes per day in bouts of at least 10 minutes each, to total of 150 to 300 minutes per week of moderate or 75 to 150 minutes of vigorous intensity activity per week (31). It is not clear whether these recommendations are appropriate or achievable for people with IPF. Similar to Nakayama et al (16) who demonstrated that patients spent only 6 minutes per day in activity with an intensity equivalent to running, our results demonstrate that patients spent 9 minutes performing moderate to high intensity activities. Only 18.4% of patients in this study performed moderate to vigorous activities for greater than 30-minute duration, consistent with activity guidelines. Time spent performing vigorous activity was predicted by 6MWD, a physiologically important prognostic predictor (32–34).

While the association between quality of life and DPA has been previously described in IPF (16, 17, 35), our study is the first to assess the impact of cough related quality of life; a relevant analysis given the high prevalence of this symptom in IPF patients. Both the overall LCQ score and the physical domain LCQ correlated with high intensity physical activity duration and steps per day. However, patient reported outcomes were not consistently associated with all parameters of DPA suggesting that how patients feel may not reflect on what they do.

The strengths of the study included a patient cohort that only included MDM-confirmed IPF, in whom SAB compliance was exceedingly high. Limitations of this study were; the SAB was not worn while performing wet activities such as showering and may have resulted in lowering the estimation of the DPA and other measures that might have contributed to impaired physical activity such as frailty scores were not collected.

Important progress has been made in the last two decades with regards to management of IPF through large clinical trials (36). These clinical trials have highlighted the strengths and limitations of study endpoints. They have also highlighted the need to develop validated surrogate endpoints that measure how a patient feels and functions, to ensure that outcomes are relevant to patients. Although clinicians responsible for the care of patients with IPF may assume that surrogate endpoints such as spirometry and six-minute walk test are reflective of DPA, the low to moderate correlation coefficients in this study demonstrate the complex multidimensional nature of physical, psychosocial and environmental factors which affect physical activity in patients. As such, direct and objective measures are required to fully understand and accurately quantify DPA.

This study has described various parameters of physical activity monitoring and their relationship with current markers of disease progression and patient reported outcomes. Longitudinal assessment of physical activity, how it changes over time and its ability to predict outcomes such as mortality will improve our understanding of whether these parameters will enhance clinical practice and monitoring of outcomes from clinical trials.

Conclusion

Our study demonstrates that physical inactivity due to its links with prognostic indices may play a crucial role in patients with IPF. Further studies are required to understand the role DPA has on prognosis of IPF, how it changes with disease progression and as to whether early detection of low levels of DPA and interventions may be beneficial.

Abbreviations

6MWD Six-minute walk distance

6MWT Six-minute walk test

AEE Active energy expenditure

ATS American Thoracic Society

BMI Body mass index

CF Cystic fibrosis

COPD Chronic obstructive pulmonary disease

CPI Composite physiologic index

DLCO Carbon monoxide diffusion capacity

DPA Daily physical activity

FEV_1 Forced expiratory volume in one second

FVC Forced vital capacity

GAP Gender, Age, and Physiology

HADS Hospital Anxiety and Depression scale

HRQOL Health-related quality of life

ILD MDM Interstitial Lung Disease Multidisciplinary Meeting

ILD Interstitial Lung Disease

IPF Idiopathic pulmonary fibrosis

LCQ Leicester Cough Questionnaire

METs Metabolic equivalence of task

MVPAD Moderate to vigorous physical activity duration

O_2Sat Oxygen saturation

PAD Physical activity duration

PFT Pulmonary function test

SAB SenseWear Armband ™

SGRQ St Georges Respiratory Questionnaire

SPD Steps per day

SPSS Statistical Package for Social Science

TEE Total daily energy expenditure

TST Total sedentary time

Declarations

Ethics approval and consent to participate

The study was granted ethical approval by the Alfred Health Office of Ethics and Research Governance (Project Reference: 107/15). Written consent was obtained from participants included in this study.

Consent for publication

Not applicable.

Availability of data and material

Data generated or analysed during this study is included in this published article and its supplementary information files. (Supplementary Table: Study Dataset).

Competing interests

The author(s) declared no potential conflict of interest with respect to the research, authorship and/ or publication of this article.

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Authors' contributions

JDP (55%): conducting the research project, statistical analysis and compilation of the manuscript.

AEH(15%): formulation of concept, review of the manuscript and the statistical analysis

ING (15%): formulation of concept, review of the manuscript and the statistical analysis

GPW (15%): formulation of concept, review of the manuscript and the statistical analysis

All authors have read and approved the manuscript.

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Tables

Table 1 Patient Characteristics (n=59)

Demographics	Age (years)	68 (7.6)
	Gender (Male %)	70
	Height (cm)	169 (9.1)
	Weight (kg)	81 (64.3-97.7)
	BMI (kg/m^2)	29 (4.7)
Symptoms (%)	Dyspnoea on exertion/Cough	92/80
Smoking history (%)	Never/Current/Ex-smoker	26/03/71
Comorbidities (%)	Emphysema	31
	Coronary artery disease	24
	Pulmonary hypertension	21
	Obstructive sleep apnoea	32
	Gastro-oesophageal reflux disease	58
	Diabetes mellitus	14
	Depression	27
	Hypertension	25
Antifibrotic therapy (%)	Nintedanib	42
	Pirfenidone	25
LTOT(%)		39
Compliance with SAB	Days	6 (5-7)
	Hours/day	23.6 (23.1-23.76)

BMI - body mass index; LTOT- long term oxygen therapy

Table 2: Physiologic and patient reported characteristics (n=59)

Pulmonary Function	FEV1 (L)	2.2 (0.5)
	FEV1 (% predicted)	78.7 (16.9)
	FVC (L)	2.6 (0.7)
	FVC (% predicted)	70.6 (16.7)
	DLCO (% predicted)	46.1 (17.3)
	FEV1/FVC (%)	82 (74.5-89.5)
6-minute walk test	Six-minute walk distance (6MWD) (m)	432.8 (129.8)
	Resting oxygen saturation (O2sat) (%)	96 (92-100)
	Nadir 6MWD O2 sat (%)	86 (75.5-96.5)
	Baseline heart rate (HR) (bpm)	76 (52-100)
	Peak heart rate HR (bpm)	112(19)
GAP stage (%)	IPF Stage	
	Stage I	45.8
	Stage II	40.7
	Stage III	13.6
Patient Reported Outcomes		
Hospital Anxiety and Depression Score	Anxiety %	
	(non-cases/ cases)	63/37
	Depression %	68/32
	(non-cases/ cases	
Leicester Cough Questionnaire	Total score	16 (8-24)
	1. Physical	5 (3-7)
	2. Psychologic	6(3-9)
	3. Social	6 (3-9)
St Georges Respiratory Questionnaire	Total score	47 (3)
	1. Symptom	49 (5-93)
	2. Activity	66 (27-105)
	3. Impact	37 (3)

Table 3 Physical Activity and Sedentary Time in 59 people with IPF

Daily Physical Activity and Sedentary Time	
Total energy expenditure (TEE) (kJ) (mean, SD)	9567 (219)
Active energy expenditure (AEE) (kJ)	2417 (434-4400)
Metabolic Equivalent of Task (MET)	1.15 (0.95-1.35)
Physical activity (PA) duration (min) (mean, SD)	188 (13.68)
Moderate to vigorous (MV) PA duration (min)	8.6 (-13.1-30.3)
Number of MVPA bouts	0.6 (-0.5-1.7)
Total sedentary time (including sleep) (min) (mean, SD)	1234.6 (122.8)
Daytime sedentary time (from 7 am to 7 pm in min)	523.7 (399.5-647.9)
Daytime sedentary bout (mean, SD)	5.1 (1.4)
Steps	3957 (300-7614)

Data are median and interquartile range, except where specified.

Table 4: Univariate linear regression: associations between clinical variables and physical activity parameters.

	Total energy expenditure (kJ)			Active energy expenditure (kJ)			Physical activity duration (min)			Moderate to vigorous activity duration (min)			Steps pe	
	R value	Adjusted *r2*	p value	R value	Adjusted *r2*	p value	R value	Adjusted *r2*	p value	R value	Adjusted *r2*	p value	R value	Adj *r2*
Age (years)	***-0.34***	***0.10***	***0.01***	***-0.30***	***0.08***	***0.02***	-0.21	0.03	0.11	-0.18	0.02	0.18	***-0.26***	***0.0***
BMI (kg/m2)	0.09	0.01	0.52	-0.25	0.04	0.06	***-0.50***	***0.24***	***<0.001***	-0.12	0.00	0.37	-0.04	0.0
Comorbidities(n)	-0.03	0.02	0.84	-0.17	0.01	0.19	-0.25	0.04	0.06	-0.07	0.01	0.58	***-0.33***	***0.1***
FEV1 (% predicted)	-0.14	0.00	0.29	0.11	0.01	0.40	0.17	0.01	0.21	0.11	0.07	0.43	***0.29***	***0.0***
FVC (% predicted)	-0.08	0.01	0.55	0.10	0.01	0.43	0.14	0.00	0.29	0.08	0.01	0.54	***0.31***	***0.0***
DLCO (% predicted)	0.17	0.01	0.21	***0.36***	***0.11***	***0.01***	***0.28***	***0.06***	***0.03***	***0.33***	***0.10***	***0.01***	***0.51***	***0.2***
6MWD (m)	***0.39***	***0.14***	***<0.01***	***0.47***	***0.21***	***<0.001***	***0.34***	***0.10***	***0.01***	***0.54***	***0.30***	***<0.001***	***0.59***	***0.3***
6MWT nadir O2sat (%)	0.00	0.02	0.97	0.12	0.00	0.38	0.15	0.01	0.26	0.11	0.01	0.43	0.22	0.0
6MWT peak HR (bpm)	0.13	0.00	0.37	0.01	0.02	0.94	-0.05	0.02	0.74	-0.03	0.02	0.86	0.12	0.0
GAP stage	-0.11	0.01	0.41	***-0.33***	***0.11***	***0.01***	***-0.31***	***0.08***	***0.02***	***-0.26***	***0.05***	***0.047***	***-0.48***	***0.2***
CPI	-0.18	0.01	0.19	***-0.31***	***0.08***	***0.02***	-0.24	0.04	0.07	***-0.27***	***0.06***	***0.041***	***-0.5***	***0.2***
HADs A	-0.10	0.07	0.45	0.01	0.02	0.95	0.05	0.02	0.70	-0.20	0.01	0.18	-0.19	0.0
HADS D	***-0.27***	***0.06***	***0.04***	-0.20	0.02	0.12	-0.13	0.001	0.31	***-0.30***	***0.07***	***0.02***	***-0.47***	***0.2***
LCQ														
1. Physical	0.20	0.02	0.14	0.21	0.03	0.12	0.12	0.00	0.37	***0.39***	***0.13***	***<0.01***	***0.34***	***0.1***
2. Psychologic	0.07	0.01	0.62	0.00	0.02	0.98	-0.04	0.02	0.79	0.21	0.03	0.11	0.18	0.0
3. Social	0.08	0.01	0.57	0.03	0.02	0.81	-0.01	0.02	0.95	0.25	0.04	0.06	0.24	0.0
4. Total	0.11	0.01	0.41	0.07	0.01	0.61	0.02	0.02	0.89	***0.28***	***0.07***	***0.03***	0.26	0.0
SGRQ														
1. Symptom	-0.02	0.02	0.91	-0.11	0.01	0.42	-0.13	0.00	0.32	-0.19	0.02	0.16	***-0.28***	***0.0***
2. Activity	-0.20	0.02	0.13	-0.21	0.03	0.12	-0.11	0.01	0.44	***-0.29***	***0.01***	***0.03***	***-0.44***	***0.1***
3. Impact	-0.07	0.01	0.61	-0.13	0.00	0.34	-0.08	0.01	0.56	***-0.30***	***0.07***	***0.02***	***-0.35***	***0.1***
4. Total	-0.12	0.00	0.39	-0.17	0.01	0.21	-0.11	0.01	0.42	***-0.31***	***0.08***	***0.02***	***-0.41***	***0.1***

BMI- body mass index; FEV1- forced expiratory volume in one second; FVC- Forced vital capacity; DLCO-carbon monoxide diffusion capacity; 6MWD- 6 minute walk distance; 6MWT end O2sat- 6 minute walk test end oxygen saturation; 6MWT end HR- 6 minute walk test end heart rate; GAP stage- gender, age physiology (composite score) stage; CPI- composite physiologic index; HADs A/D- hospital anxiety and depression score anxiety/ depression; LCQ- Leicester Cough Questionnaire; SGRQ- St. Georges Respiratory Questionnaire

Table 5: Stepwise multiple regression to identify predictors of physical activity in IPF

Stepwise Multiple Regression				
Total Energy Expenditure				
	B	p value	95% confidence interval	
			Lower bound	Upper bound
Constant	12144	0.00	7468	16821
6MWD	5.2	0.01	1.4	9.0
Age	-76.2	0.02	-137.8	-14.6
R	0.49	Adjusted r^2	0.24	
Active Energy Expenditure				
	B	p value	95% confidence interval	
			Lower bound	Upper bound
Constant	9136	0.001	3861	14410
6MWD	3.0	0.06	-0.14	6.1
Age	-86.8	0.001	-138.5	-35.1
BMI	-118.4	0.005	-199.8	-36.8
DLCO	29.6	0.011	7.1	52.0
R	0.66	Adjusted r^2	0.39	
Physical Activity Duration				
	B	p value	95% confidence interval	
			Lower bound	Upper bound
Constant	947.8	0.00	683.3	1212.6
BMI	-14.8	0.00	-19.3	-10.3
Age	-6.3	0.00	-9.2	-3.4
DLCO	2.1	0.001	0.9	3.3
R	0.74	Adjusted r^2	0.54	
Moderate to vigorous PA duration				
	B	p value	95% confidence interval	
			Lower bound	Upper bound
Constant	-30.5	0.01	-53.9	-7.2
6MWD	0.1	0.00	0.1	0.2
R	0.54	Adjusted r^2	0.28	
Steps				
	B	p value	95% confidence interval	
			Lower bound	Upper bound
Constant	-3435	0.007	-5905	-966
6MWD	10.8	0.00	5.6	16
DLCO	59.7	0.003	21.2	98.2
R	0.67	Adjusted r^2	0.42	
Total sedentary time				
	B	p value	95% confidence interval	
			Lower bound	Upper bound
Constant	737.3	0.00	569.9	904.7
BMI	13.3	0.00	8.3	18.3

IPF stage	64.1	0.001	28.1	100.2
R	0.65	Adjusted r^2	0.4	

6MWD- 6-minute walk distance; 6MWT end HR- 6-minute walk test end heart rate; BMI- body mass index; DLCO- carbon monoxide diffusion capacity; IPF stage- gender, age physiology (GAP) stage

Figures

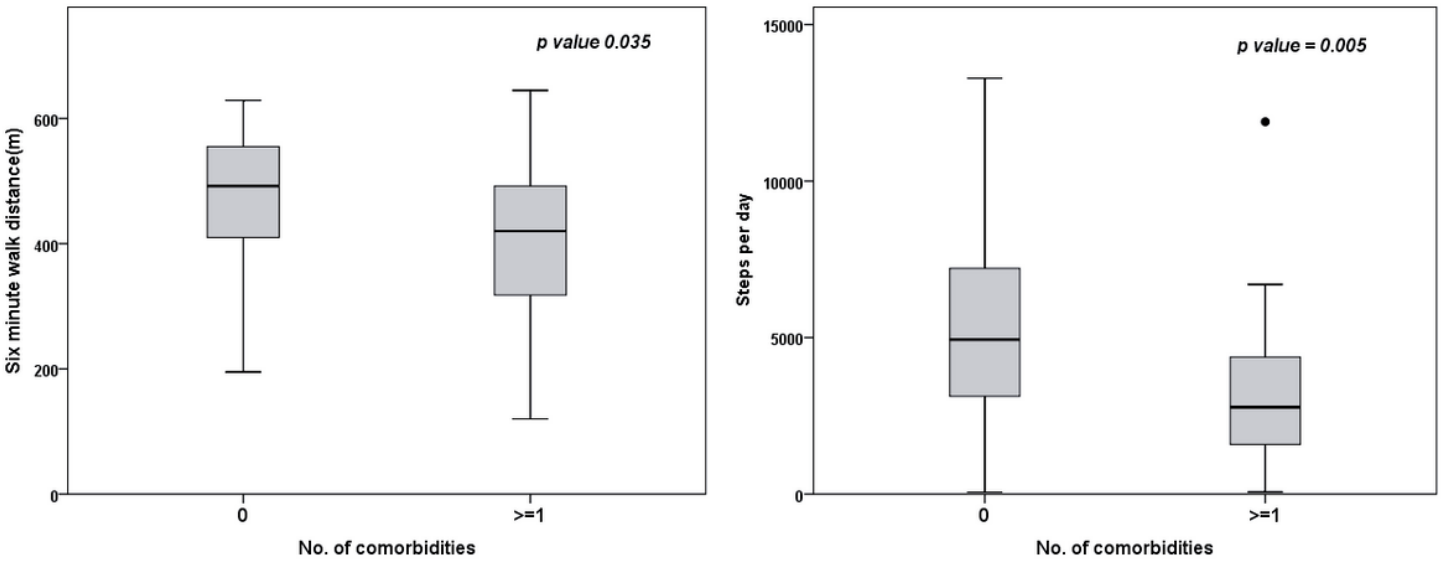

Figure 1

Exercise and SPD related to comorbidities

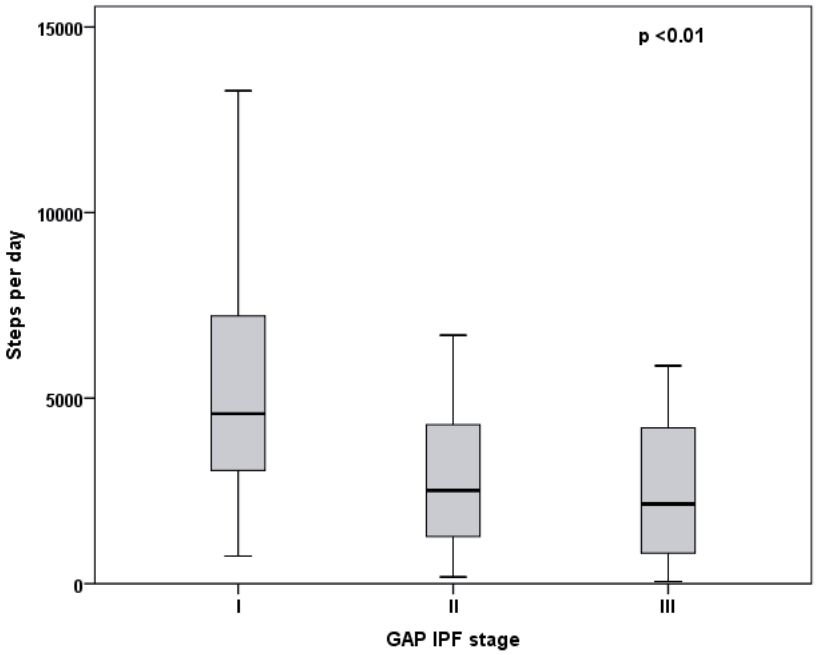

Figure 2

Steps per day according to GAP index

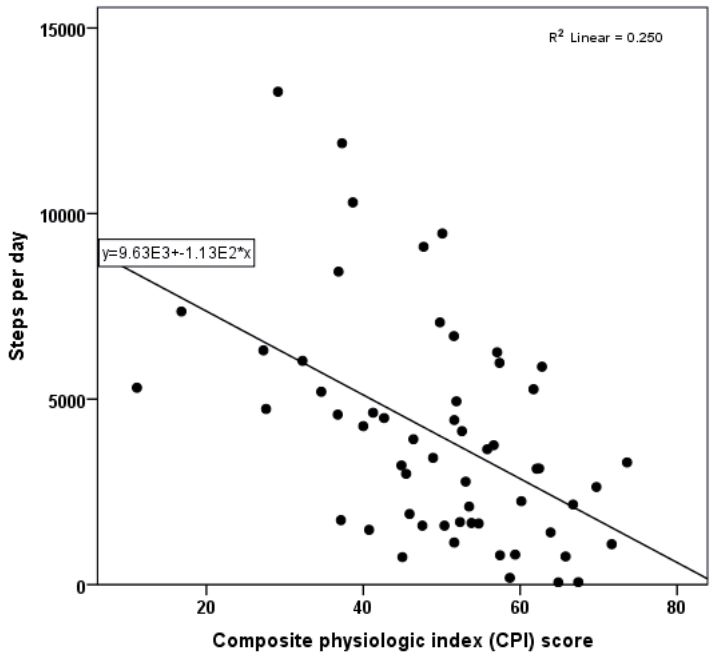

Figure 3

Linear relationship of steps per day and CPI

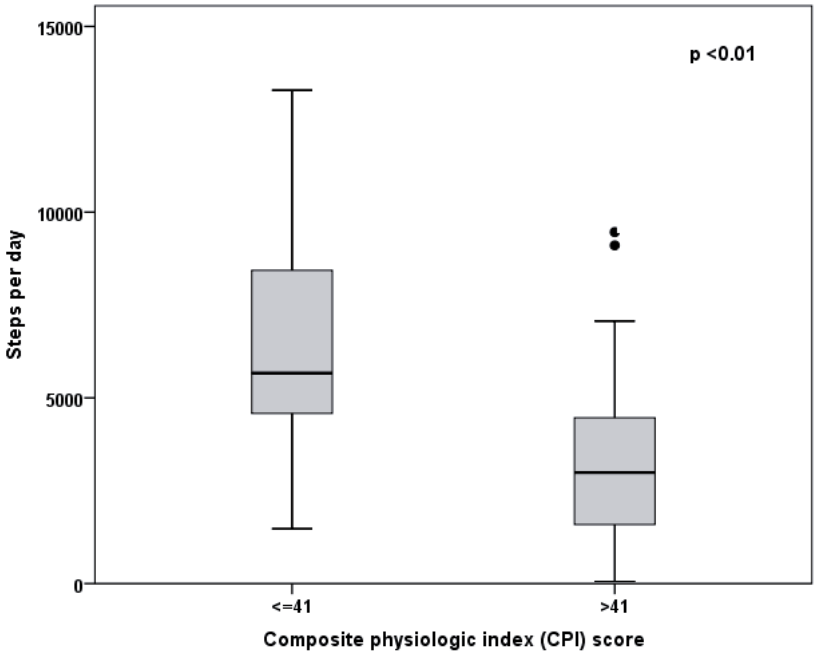

Figure 4

Steps per day according to CPI score

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- STROBEchecklistcrosssectional.doc