Physical Activity and Sedentary Behavior in Adults With Cystic Fibrosis: Association With Aerobic Capacity, Lung Function, Sleep, Well-Being, and Quality of Life

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BACKGROUND: Physical activity (PA) and sedentary behavior (SB) have marked impact on key prognostic indicators such as aerobic capacity and lung function in people with cystic fibrosis (CF) and may have associations with sleep, well-being, and health-related quality of life (HRQOL). METHODS: This observational study assessed PA, SB, aerobic capacity, spirometry, sleep, well-being, and HRQOL in adults with CF at University Hospital Limerick. PA and SB were assessed using an accelerometer that was worn for 7 days. A cardiopulmonary exercise test assessed aerobic capacity. Spirometry was performed according to American Thoracic Society guidelines. Well-being was measured by the AWESCORE, sleep quality by the Pittsburgh Sleep Quality Index (PSQI), and HRQOL using the CF Questionnaire-Revised. RESULTS: Thirty-three participants (13 males/20 females) were recruited. Mean age was 26.2 y (± 7.1 SD), with mean FEV_1 72.9% of predicted (± 26.2 SD). Mean step count was 7,788 (± 3,583 SD). Over 75% of participants did not reach recommended PA targets (> 10,000 steps), with females being 25.5% less active than males. The PSQI indicated 48.5% of participants scored > 5, indicating poor sleep quality. Number of steps and SB demonstrated a moderate significant correlation with FEV_1 (r = 0.45, P = .030; r = −0.37, P = .043, respectively) and sleep quality (r = −0.85, P < .001; r = 0.77, P < .001, respectively). $\dot{V}_{O_2}$ peak expressed relative to body weight, and as a percentage of predicted, was significantly positively correlated with step count (r = 0.48, P = .007; r = 0.42, P = .02, respectively) but did not correlate with SB (P = .96). $\dot{V}_{O_2}$ peak (L/min) strongly correlated with FEV_1 (r = 0.75, P < .001). CONCLUSIONS: Most participants did not meet PA targets. PA levels correlated to aerobic capacity, FEV_1, and self-reported sleep quality, and this should be considered in longitudinal studies and in PA interventions. *Key words: Cystic fibrosis; physical activity; sleep; well-being.*
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Introduction

Cystic fibrosis (CF) is an inherited, lifelong, multisystem disease.[1] CF has a mean prevalence of one in 13,500 in the European Union.[2] It is caused by mutations in the CF transmembrane conductance regulator (CFTR) gene that is responsible for encoding the CFTR epithelial chloride channel.[3] There is significant morbidity and mortality associated with the disease as a result of recurrent pulmonary exacerbations and subsequent decline in lung function capacity.[4] Previously, CF was considered a childhood disease; however, with advancements in treatments and management, this has led to an increase in life expectancy to a median age of 48.4 y in 2019.[5] This shift in demographics, combined with innovative development of novel therapeutic care, which specifically targets the underlying pathophysiology, is advancing CF care.

Regular physical activity (PA) among people with CF (PWCF) can positively impact on the course of the disease.[6] PA is widely regarded as an important component of CF care. PA levels are directly related to aerobic fitness in PWCF.[7,8] Lower mortality rates,[9] less decline in lung function,[10] reduced hospital length of stay,[11] improved sleep quality,[12] and improved health-related quality of life (HRQOL)[13] are observed in PWCF who have better physical fitness. As a result, previous literature suggests that PA assessment is important in PWCF in order to guide clinical practice.[14-16] Objective assessment of PA is recommended as this is more accurate and reliable than self-reported measures.[17]

Sedentary behavior (SB) is an independent risk factor for cardiometabolic diseases in children and in youth.[18] Previous research has found no significant difference in sedentary time among PWCF when compared to healthy counterparts.[19,20] However, greater daytime SB has been found to result in shorter sleep time at night.[21] These authors also reported that a longer total sleep time was associated with less sedentary time the following day.[21] Poor sleep quality in CF has been associated with lower mood[22] and reduced HRQOL.[23] It has been identified across all ages of PWCF, particularly in those with more severe disease.[24] There are a number of reasons for sleep disturbances including coughing,[25] nocturnal oxygen desaturation,[26] hypoventilation,[24] and upper-airway obstruction.[27] It is well documented that PA is associated with improved sleep, and evidence is mounting to support PA as a nonpharmacologic treatment for poor sleep.[28] However, research also suggests that poor sleep may lead to low PA levels, suggesting a bidirectional relationship between PA and sleep quality and quantity.[28]

There is a significant treatment burden associated with CF, including issues with adherance[29] and psychological well-being,[30] especially in adults that are balancing family, work, and education as well as managing their chronic disease.[31] HRQOL is thus a key consideration in PWCF and has been increasingly recognized as an important clinical outcome in recent years.[32] HRQOL has enabled a prediction of survival in PWCF.[33]

The primary aim of this study was to evaluate PA and SB levels in PWCF and determine their association with aerobic capacity, lung function, and sleep. Secondary aims included determining if PA correlated with HRQOL and well-being in PWCF.

QUICK LOOK

Current knowledge

Physical activity (PA) is a key component in the management of cystic fibrosis (CF). With an increasing life expectancy of adults with CF, this highlights the importance of the assessment and monitoring of PA behavior and its impact on improving long-term health.

What this paper contributes to our knowledge

Most adults with CF did not meet PA targets (75%). Females were 25% less active than males. PA correlated to aerobic capacity, FEV_1, and self-reported sleep quality in adults with CF, which suggests that a bidirectional relationship may exist between these factors.

Methods

Study Design and Methods

This was an observational study design. This study followed the STROBE standardized reporting guidelines to conduct and report the study.[34] Consent and mechanisms relating to data controlling and processing were compliant with the EU General Data Protection Regulation 2016/679 and in compliance with the Data Protection Act 2018 (Section 36[2] [Health Research] Regulations 2018). Ethical approval was obtained from the University Hospital Limerick Research Ethics Committee (approval number 054/18).

Participants

Thirty-three participants were recruited from the adult CF out-patient unit, University Hospital Limerick, Ireland. Inclusion criteria were age ≥ 18 y, confirmed diagnosis of CF (based on CF-causing mutations and/or a sweat chloride concentration during 2 tests of > 60 mmol/L), and clinically stable CF (ie, not experiencing a pulmonary exacerbation in the last month). For the purpose of this study, pulmonary exacerbation was defined as acute or subacute worsening of respiratory symptoms that warrants change in

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treatment (ie, new oral or intravenous antibiotics), as per previous research by Savi et al.[35] Exclusion criteria were $FEV_1 < 25\%$ of predicted; patients on the waiting list for lung transplantation or prior lung transplantation; patients dependent on supplemental oxygen for exercise; adults with CF who were pregnant; patients with any cardiac, neurological, or musculoskeletal impairment that impacted on their ability to be physically active; participation in another clinical trial up to 4 weeks prior to their PA assessment; and patients with an exacerbation in the 4 weeks prior to the study. PWCF could undergo testing after this 4-week period and once deemed clinically stable to participate in the study by the respiratory consultant (BC). Sample size was calculated based on previous research with similar study designs and outcome measures. A total of 30 participants were required to achieve power based on a significant association between PA and $\dot{V}_{O_2}$. Significance was defined as 0.05.

Outcome Measures

activPAL. The activPAL3 (PAL Technologies, Glasgow, Scotland) is a small accelerometer that is placed on the anterior thigh and records step count and SB in a single-unit device. The accelerometer model is triaxial, and the sampling frequency is 20 Hz with a dynamic range of $\pm$ 2 g. All participants wore the accelerometer to assess PA and SB over 7 d. The device was placed one-third of the distance between the patella and inguinal crease at the midline of the anterior surface of the participant's right thigh and secured with Tegaderm. Data were included if at least 4 full d (at least 3 weekdays and one weekend d) of measurements with a minimum of 10 h for the weekdays and 10 h for the weekends were measured.[36] Data were downloaded and analyzed using proprietary algorithms. Activity was expressed in 2 ways: (1) average step count per day and (2) daily time spent in SB. SB consists of both lying and sitting postures, as the accelerometer cannot distinguish between these two positions. The following parameters were applied to classify PA based on the number of daily steps reported: sedentary ($<$ 5,000), low active (5,000–7,499), somewhat active (7,500–9,999), active ($\geq$ 10,000), and highly active ($>$ 12,500).[37]

Cardiopulmonary Exercise Test. A cardiopulmonary exercise test (CPET) was conducted utilizing a ramp protocol on a cycle ergometer. The ramp protocol ensures that work rate is progressively and linearly incremented until maximal effort is achieved.[38] The CPET consisted of a 3-min warm-up (unloaded pedaling) followed by a stepwise increase in load according to the participant's height. The increments in resistance were based on height, increasing by 10, 15, or 20 W for subjects shorter than 125 cm, 125–150 cm, or taller than 150 cm. This test was continued until exhaustion. The CPET was conducted using the Medisoft Ergocard Professional (Medisoft, Sorinnes, Belgium) CPET equipment and analyzed by ExpAir, the Medisoft software. Participants were encouraged verbally throughout the test to attain a maximal effort. Testing was concluded when participants could not maintain a pedaling frequency of 40 rpm. Peak oxygen uptake ($\dot{V}_{O_2}$ peak) was expressed per kg body mass and also expressed as percentage of predicted.[39] All participants had to attain at least one of the following maximal exercise criteria to be included in the analysis: plateau in $\dot{V}_{O_2}$, peak heart rate $>$ 100% predicted, $\dot{V}_E$ peak $\leq$ 85% maximum voluntary ventilation, respiratory exchange ratio $>$ 1.05.[40] The modified Borg scale was used to monitor shortness of breath during the test.[40]

Spirometry. Spirometry was performed according to American Thoracic Society standard techniques[41] using the CareFusion MicroLab spirometer (BD, Franklin Lakes, New Jersey). FEV_1 and FVC were collected. Values were expressed as a percentage of the predicted value for height, sex, and age for adults.[42]

Pittsburgh Sleep Quality Index. The Pittsburgh Sleep Quality Index (PSQI) is a self-rated 19-item questionnaire that measures the quality and patterns of sleep in adults and has previously been found to be effective in assessing sleep quality in CF.[43] The sleep scores are added together to attain a score ranging from 0–21, with higher scores indicating poor sleep quality. In order to distinguish between good and poor sleepers, a global PSQI $>$ 5 yields a sensitivity of 89.6% and a specificity of 86.5%.[44]

CF Questionnaire-Revised. The CF Questionnaire-Revised is a fully validated disease questionnaire consisting of 52 items across 9 domains of functioning that have been identified by, and are of importance to, adolescents and adults with CF.[45] This questionnaire is valid, sensitive, and has strong test-retest reliability.[46]

AWESCORE. This questionnaire assesses state of wellness to assist in providing best health care.[47] There are 10 questions, which are scored from 0–10. Total scores range from 0–100, with higher scores indicating good state of wellness. This is a reliable tool for measurement of multidimensional wellness in adults with CF that is appealing to patients.[47]

Procedure

Eligible participants attended the adult CF unit where a CF physiotherapist explained the study procedure, and written consent was attained. The accelerometer was applied, and participants were instructed to wear it continually for 7 d. At the end of this 7-d period, participants returned to the

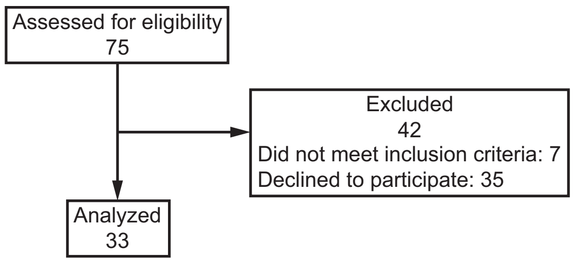

Fig. 1. Flow chart.

adult CF unit for exercise testing, spirometry, and completion of questionnaires. Lung function and anthropometric measurements of the participants were assessed. Height and body mass were determined in light exercise clothing without shoes. Data were downloaded from the accelerometer. After 30 min of rest, a CPET was conducted, as previously described. Participants were given a rest period after their maximal exercise test, and the following questionnaires were then completed: PSQI, CF Questionnaire-Revised, and the AWESCORE. These questionnaires were completed by the participants independently. A physiotherapist was available to answer any queries the participant had.

Statistical Analyses

Participant characteristics, PA, lung function, and exercise test results were analyzed depending on the distribution of the data. Normally distributed variables were presented as mean (SD), whereas variables with a skewed distribution were presented as median (interquartile range). The correlation between PA and aerobic capacity, sleep, and HRQOL was evaluated by the nonparametric Spearman correlation coefficient. The strength of this relationship was categorized as small (r < 0.3), medium (r = 0.3–0.5), or large (> 0.5).[48] The significance level for all tests was set at 5%, with a *P* value < .05 considered to be significant. An independent *t* test was used to compare means between male and female step count. Multivariable linear regression was used to quantify value of the relationship between the independent variables to predict the dependent variable (number of steps). Variables significant at the correlation stage were brought forward to the regression model. The SPSS V.27 statistical package (IBM, Armonk, New York) was used for all analyses.

Table 1. Baseline Characteristics

Sex, male/female	13/20
Age, y	26.2 ± 7.1
BMI, kg/m^2	22.4 ± 3.4
FEV_1, L	2.6 ± 1.2
FEV_1, % predicted	72.9 ± 26.2
FVC, L	3.7 ± 1.3
FVC, % predicted	86.3 ± 27.7
PI:PS	28:5
Delta F508 homozygous:heterozygous, %	45:55

Participant characteristics (except sex) are presented as mean ±SD.
BMI = body mass index
PI = pancreas insufficiency
PS = pancreas sufficiency

Results

Out of 40 participants who initially agreed to participate in this study, 33 met the inclusion/exclusion criteria (Fig. 1). Sixty-one percent were female with a mean age 26.2 y (± 7.1 SD) and mean FEV_1 of 72.9% (Table 1).

Physical Activity

Over 75% (25/33) of participants did not reach recommended PA targets (> 10,000 steps). Mean (± SD) step count was 7,788 (± 3,583). Six participants were classified as sedentary (< 5,000 steps/d); 12 participants were low active (5,000–7,499 steps), 7 were somewhat active (7,500–9,999), and one active (≥ 10,000), whereas 7 achieved over 12,500 steps (highly active). Mean step count for males was significantly greater than females (9,211 ± 3,929 SD vs 6,864 ± 2,887 SD, *P* =.02). Mean sedentary time was 18.6 (± 2.1 SD) h per day and was similar for males and females. Number of steps and SB demonstrated a moderate significant correlation with FEV_1 (r = 0.45, *P* = .03; r = −0.37, *P* = .043, respectively).

Aerobic Capacity. $\dot{V}_{O_2}$ peak expressed relative to body weight, and as a percentage of predicted, was significantly positively correlated with step count (r = 0.48, *P* = .007; r = 0.42, *P* = .02, respectively) but did not correlate with SB (*P* = .96). $\dot{V}_{O_2}$ peak (L/min) strongly correlated with FEV_1 (r = 0.75, *P* < .001).

Sleep. The mean PSQI score was 5.7 (± 3.9 SD), which is suggestive of overall poor sleep quality. Sixteen (48.5%) participants scored > 5, indicating poor sleep quality. A relationship was found between sleep quality and PA for the entire group, whereby poor sleep quality was strongly and significantly negatively correlated with low step counts (r = −0.85, *P* < .001) and strongly positively correlated with higher sedentary time (r = 0.77, *P* < .001.). All participants with > 7,000 steps had good self-reported sleep quality (PSQI < 5) (Fig. 2).

Well-being. Mean AWESCORE was 69.5 (± 12.6 SD), indicating very good levels of well-being overall. Well-being did not correlate with number of steps (r = 0.32, *P* = .09) or SB (r = −0.30, *P* > .99).

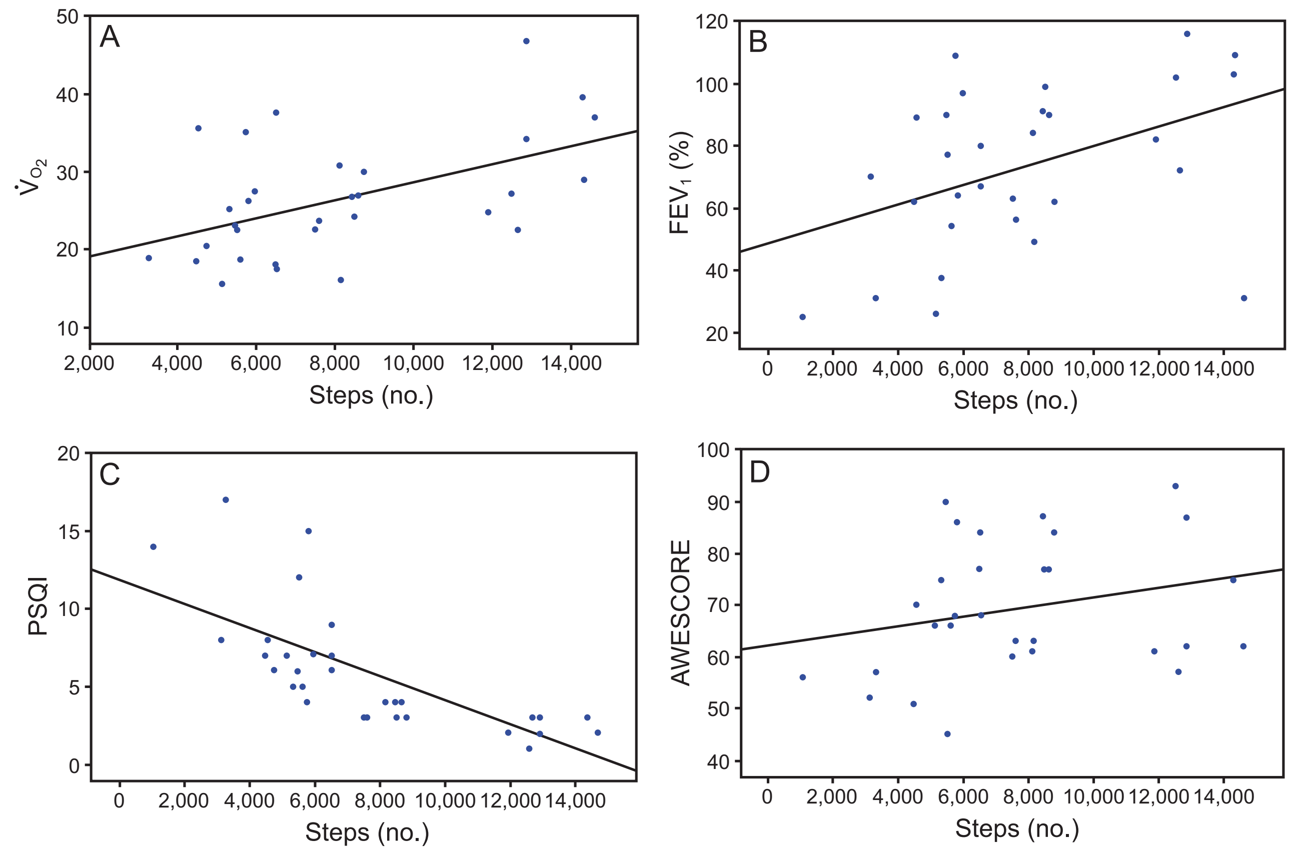

Fig. 2. Scatterplot illustrating the relationship between the number of steps and A: $\dot{V}_{O_2}$ (kg), B: FEV1, C: PSQI, and D: AWESCORE.

Multivariable linear regression was carried out to investigate the relationship between the number of steps and sex, age, PSQI, $\dot{V}_{O_2}$, and FEV_1. The R2 value was 0.624; therefore, 62.4% of the model can be explained by these variables (P = .001). The PSQI remained significant in the model (Table 2).

Discussion

The aim of this study was to objectively assess PA and SB levels in PWCF and determine the relationship with aerobic capacity, lung function, sleep, well-being, and HRQOL. In this prospective, observational study we found that 75% of participants did not meet PA guidelines. Lower step count was significantly correlated to lower FEV_1, lower aerobic capacity, and poorer self-reported sleep quality. As this is an observational study, we cannot assume causation in the relationship between PA, SB, and these variables, and it is likely that a bidirectional relationship occurs in all cases. However, further prospective research that we are currently conducting will provide clarity on the nature of these relationships.[49] In a systematic review and meta-analysis in PWCF, Shelley et al[16] also found that participants did not achieve recommended PA guidelines or step count targets in most studies. We also found that females were 25% less active than males, which is corroborated by previous research in a CF population.[11,50] This highlights the need to establish effective interventions to increase PA particularly in females with CF.

Table 2. Multivariable Linear Regression Model Between Number of Steps and Demographic and Clinical Variables

	Standardized Coefficients (β)	95% CI	P
Age	0.049	−120.43 to 169.76	.73
Sex	0.259	−177.39 to 3,978.67	.07
FEV_1	0.037	−45.86 to 55.93	.84
$\dot{V}_{O_2}$	0.165	−38.35 to 107.44	.34
PSQI	−0.634	−867.12 to −295.85	< .001

PSQI = Pittsburgh Sleep Quality Index

Our study found that low FEV_1 was associated with fewer steps/d (r = 0.45, P = .01) and higher sedentary time (r = −0.37, P = .043). This is similar to a recent study that also found lower FEV_1 is associated with fewer steps/d (r = 0.46, $P = \leq .01$) and more SB (r = −0.44, $P = \leq .01$) in 109 PWCF.[51] This is further supported by Cox and colleagues[11] who also found that less PA was linked to FEV_1.

Troosters et al[52] found that there was a trend for a relationship between the number of steps/d and lung function ($r = 0.39$, $P = .08$). However, PA was only assessed in a subgroup of 20 participants in that study.[52] The effect of exercise interventions on both PA and FEV_1 has been previously investigated in both short- and long-term studies. An in-patient intervention conducted among 66 PWCF found a significant improvement in PA and FEV_1.[53] Similarly, a 3-y home exercise program also found a significant improvement in self-reported PA and a slower rate of decline in lung function in 65 PWCF.[54] Therefore, the association between PA and FEV_1 may be an important consideration in CF management, as well as, future intervention studies.

A significant correlation was found between PA and aerobic capacity. Previous research supports this finding.[7,8,12] In contrast, one study with a similar sample size ($N = 30$) did not find an association between the two.[39] However, this study was conducted in a younger population, with milder CF disease, and used a self-reported measure of PA (activity questionnaire), which may be limiting factors to the detection of the relationship. Several exercise interventions conducted in this population have found that an increase in PA resulted in an improvement in aerobic capacity.[53,55,56] It is, therefore, possible to suggest that improving PA may result in an improvement in aerobic capacity.

The results in our study show that a relationship exists between steps/d and sleep quality in PWCF. Furthermore, multivariable linear regression analysis highlighted sleep quality was the variable with the greatest association with step count. Cox and colleagues[12] found that fragmented sleep was associated with less PA in PWCF,[12] whereas a longitudinal study by Dietz-Terjung et al[51] found that PA influenced sleep quality, whereby participants undertaking vigorous intensity PA had better sleep quality.[51] Poor sleep affected 48.5% of PWCF in our study. Interestingly, the more active participants in this study (those achieving > 7,000 steps/d) did not report any issues with sleep quality.

There was no relationship identified in this study between PA and HRQOL or well-being. In contrast, an observational study in COPD found that PA and HRQOL were significantly correlated; however, it should be noted that average step count in this COPD population was < 48% our daily average. Cox and colleagues[57] previously reported that PA interventions did not significantly improve HRQOL in PWCF. It was suggested that this may be as a result of CF being a more complex multisystem disease in comparison to other respiratory populations.[57]

PA has numerous benefits among PWCF; however, this cohort did not reach PA guidelines, with females being significantly less active than males. Future interventions should focus on exploring barriers and facilitators to improve PA in this patient population. PA and SB are two individual risk factors for health.[58] Sitting time and screen time (quantified as time spent in front of any screen device) are two of the primary indicators used in quantifying time spent sedentary.[58] PA and SB levels correlate to aerobic capacity and self-reported sleep quality, and this should be considered in PA interventions. While there has been a focus on PA assessment and PA interventions in PWCF in recent years, there is little evidence on the knowledge and understanding of SB in PWCF; and therefore, this should be assessed in future research. As stated, it is possible that a bidirectional relationship may exist between these outcomes. Future research should consider longitudinal studies with larger population sizes to further elucidate this relationship. We are nearing completion of a prospective study in this population to explore these relationships and clarify causation.

While some interesting findings were found, there are limitations to this research. This was an observational study. While sample size was calculated and attained, the participants in this study were a sample of convenience that may limit generalizability of findings. We did not objectively measure sleep due to time and equipment constraints. While the accelerometer is valid and reliable for PA assessment in PWCF, it cannot distinguish between patterns of SB and includes sleep as well as conventional wake-time SB. Therefore, this limits the detailed analysis of SB. There were five variables included in the regression model. While this breaks the rule of thumb that a minimum of 10 outcome events is required per predictor variable, a previous simulation study suggests this may be too conservative.[59]

Conclusions

In conclusion, PA was significantly correlated to aerobic capacity, lung function, and self-reported sleep quality in subjects with CF. Most of our cohort failed to meet recommended PA targets, with females being less active than males. Future studies should consider longitudinal research with large sample sizes to determine if a bidirectional relationship exists between these key components of health.

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