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Longitudinal changes in the 6-minute walk test and the Glittre-activities of daily living test in adults with cystic fibrosis

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Abstract

With the increasing use of highly effective modulator therapy (HEMT) in adults with cystic fibrosis (awCF), it is necessary to determine the evolution of the most dynamic physiological markers of this disease, such as the 6-minute walk test (6MWT) and the Glittre-activities of daily living test (TGlittre). The present study aimed to evaluate the 1-year changes in the 6-minute walking distance (6MWD), TGlittre time, and quality of life (QoL) in awCF before the initiation of HEMT and to determine the impact of habitual physical activity (HPA) and chest physiotherapy (CP). This longitudinal study enrolled 24 awCF who completed the 6MWT and TGlittre. Pulmonary function tests, handgrip strength (HGS), and the Cystic Fibrosis Questionnaire-Revised (CFQ-R) were conducted. Measurements were collected at baseline (T1) and 1 year later (T2). The median body mass index increased between T1 and T2 [19.8 (18-24) *vs*. 21.4 (19-24) kg/m², p=0.038]. TGlittre time decreased both in relation to the absolute values [3.10 (2.52-3.39) *vs*. 2.40 (2.00-3.00) minutes, p=0.001] and in relation to the predicted values [127 (116-150) *vs*. 108 (102-140) % predicted, p=0.001]. Although there was no increase in 6MWD relative to the predicted values, it increased relative to the absolute values [545 (463-654) *vs*. 617 (540-658) m, p=0.041]. In relation to the group that did not engage in HPA, individuals who had HPA showed an increase in HGS between T1 and T2 [7.1 (0-20) *vs*. 0 (-12-3) kgf, p=0.031]. In relation to the group that did not undergo CP, individuals undergoing CP showed an increase in the "treatment burden"-CFQ-R between T1 and T2 [16.1 (-3-18) *vs*. -11.2 (-28-1) points, p=0.049]. In conclusion, awCF performed better on TGlittre than on 6MWT. They experienced an improvement in body composition. HPA was correlated with peripheral muscle strength, as were CP and QoL.

Key words: cystic fibrosis, exercise, pulmonary function tests, muscle.

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Introduction

Cystic fibrosis (CF) is an autosomal recessive disease caused by mutations in the *CFTR* gene. It affects the pulmonary, gastrointestinal, and musculoskeletal systems [1]. In recent years, among adults with CF (awCF), the prognosis of CF has improved due to continuously updated protocols and treatments [2]. Recent discoveries about *CFTR* mutations paved the way for the development of highly effective modulator therapy (HEMT), which is available for up to 85% of all individuals with CF aged 12 years and older with at least one F508del mutant allele [2,3]. In Brazil, however, only 60% of individuals with CF have at least one F508del allele, so this country has fewer candidates for HEMT [4]. Despite improvements in health outcomes, CF remains a life-shortening disease, with respiratory failure as the leading cause of death. In this sense, lung function is one of the main primary outcome measures for clinical trials and regulatory approval of new therapies [5]. Lung function, as a single outcome measure, only provides a measure of lung health, so we must consider the impact of other systems, such as the cardiovascular and musculoskeletal systems.

Although cardiopulmonary exercise testing (CPET) is a major standard test for evaluating functional capacity during exercise, tests of functional capacity at submaximal exercise have been increasingly used in clinical practice as an outcome measure in awCF [6,7]. The 6-minute walk test (6MWT) is a simple, reproducible, and reliable submaximal exercise test used to assess functional capacity during exercise in awCF [7,8]. In addition to being a viable and inexpensive test, the 6MWT reflects the general fitness of the individual and has a good correlation with prognosis, especially in awCF with worse lung function [6]. The CF Foundation recommends annual exercise testing using the 6MWT in those with a predicted forced expiratory volume in 1 second (FEV_1) <40% and referral to lung transplantation (LTX), regardless of FEV_1, when the 6-minute walk distance (6MWD) is <400 m [9]. In recent decades, interest in the 6MWT in awCF has increased, not only in LTX candidates but also as a prognostic marker of CF severity [10].

Although the 6MWT is widely used in clinical practice, the need for a 30-m corridor limits its use in general wards or outpatient settings [11]. Unfortunately, the 6MWT incorporates only walking as a representative of the activities of daily living (ADLs) in awCF (American Thoracic Society Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories, 2002). In addition, the relationship between 6MWD and maximum oxygen uptake (VO_{2max}) as measured by CPET is not linear – this is described as a ceiling effect, *i.e.*, after a certain distance, minimal increases in 6MWD are associated with substantial changes in VO_{2max} [12,13]. The Glittre-activities of daily living test (TGlittre) was developed [12] to evaluate the ADLs of individuals with chronic respiratory disease and is a reliable tool both for children and adolescents [14] and for awCF [7]. In addition to the fact that the TGlittre incorporates several ADLs that require the action of both the upper and lower limbs, the TGlittre can induce physiological changes, such as those observed during the 6MWT, in approximately half as much time [15-17]. Our group recently showed that in awCF, the TGlittre is more effective than the 6MWT for detecting limitations during exercise, and there is a moderate relationship between the TGlittre time and the 6MWD [7].

Habitual physical activity (HPA) and chest physiotherapy (CP) are important aspects of treating individuals with CF, as they can result in improved health-related measures of physical fitness. HPA and CP can positively impact quality of life (QoL) and prognosis [18]. HPA involves ADLs and recreation, which increase energy expenditure compared to rest, in contrast to exercise, which is purposeful and structured for improvements in physical conditioning and airway clearance [19]. CF-related comorbidities should be considered when recommending HPA, but individuals with CF should seek to maximize their HPA, reduce their sedentariness, and participate in structured physical training [20]. Another approach that should be encouraged is CP, as it leads to greater sputum clearance, reduces the recurrence of lung infections, slows the progression of lung destruction, improves lung function, and increases the QoL of individuals with CF [21].

Multiple outcome measures, including functional capacity during exercise and QoL, are required to obtain a broader and more accurate assessment of CF progression and to quantify the burden of disease. Recently, HEMT, which is a type of targeted therapy that acts directly on the CFTR channel, has been increasingly used. More specifically, HEMT improves lung function, respiratory muscle strength, and QoL in awCF, although many awCF living in Brazil are not candidates for HEMT [1,4]. Furthermore, before starting HEMT, it is necessary to determine the evolution of outcome measures in this population, especially the use of more dynamic physiological markers of CF severity, to quantify its impact on disease burden. Thus, in this study, we aimed to evaluate the 1-year changes in the 6MWD, TGlittre time, and QoL in awCF before the initiation of HEMT and to determine the impact of HPA and CP.

Materials and Methods

Study design, participants and ethics

A longitudinal observational study was conducted between May 2022 and March 2024 with 24 awCF (out of 34 eligible individuals) who were regularly followed up at the Piquet Carneiro Polyclinic of the State University of Rio de Janeiro, Rio de Janeiro, Brazil. The diagnosis of CF was made based on the following parameters: i) clinical presentation of CF plus a positive sweat chloride test; ii) clinical presentation plus borderline sweat chloride results plus two *CFTR* mutations that cause CF; and iii) an undefined or unknown *CFTR* genotype based on genetic analysis plus positive physiological CFTR tests indicating CFTR dysfunction [22]. The exclusion criteria were as follows: any acute exacerbation in the last 3 weeks; physical disabilities hindering the performance of field tests; referral for LTX; abandonment of CF treatment; and loss to follow-up or death during the 1-year observational period. HPA and CP were self-reported by all participants. HPA only includes recreational activities that increase energy expenditure compared to that at rest [19]. CP was defined as the use of procedures to improve clearance, both through positive expiratory pressure devices and standardized chest maneuvers guided by physical therapists, as well as effective breathing exercises [23].

This study was conducted in accordance with the Declaration of Helsinki, and written informed consent was obtained from the participants. This study was approved by the Research Ethics Committee of the Pedro Ernesto University Hospital of the State University of Rio de Janeiro under protocol number CAAE-93586318.0.0000.5259.

Measurements

QoL was assessed by the Cystic Fibrosis Questionnaire-Revised (CFQ-R). This questionnaire has 50 items divided into 12 generic and disease-specific scales. The CFQ-R measures several domains, including the physical and respiratory domains. The scores in each domain range from 0 to 100, with lower scores indicating worse QoL and scores >50 reflecting good QoL [24].

Handgrip strength (HGS) was evaluated with a manual hydraulic dynamometer (Jamar, Model 5030 J1, Sammons Preston Rolyan, Bolingbrook, IL, USA). The dominant upper limb was positioned with the shoulder in neutral rotation, the elbow in 90° flexion, the forearm in neutral position, and the wrist in slight extension. The participants were asked to squeeze the dynamometer as hard as possible. Three measurements were performed at 30-second intervals, and the mean of the three measurements was taken [25].

The pulmonary function test consisted of spirometry and measurement of respiratory muscle strength. The spirometric test was performed with a volume spirometer (Vitatrace VT, Codax Ltda., Rio de Janeiro, Brazil). The procedures followed previously established guidelines [26], and the results are expressed as percentages of the predicted values [27]. Respiratory muscle strength was measured using a digital pressure gauge (MicroRPM; Vyaire Medical Inc., Mettawa, IL, USA) as previously recommended [28].

The 6MWT was performed as previously described [29]. Participants were instructed to walk the greatest possible distance in 6 minutes back and forth along a 30-m flat stretch, marked on the ground with cones at both ends. Blood pressure, heart rate, respiratory rate, and peripheral oxygen saturation (SpO_2) were measured before and at the end of the 6MWT. 6MWT was immediately discontinued if SpO_2<80%, exhaustion, chest pain or intolerable cramps occurred. The 6MWT was performed a second time after a 30-minute rest, and the highest 6MWD was taken for comparison to the predicted values [30].

TGlittre was performed as originally proposed [11] in a 10-m circuit. The participant started in the sitting position. The participant stood up, walked straight, went up and down two steps, and walked to a bookshelf with two shelves, whose height was adjusted for each participant. Then, the participants moved 3 objects of 1 kg, one by one, from the top shelf to the bottom shelf, then to the

floor and back to the bottom shelf, and finally back to the top shelf. After this activity, the participant walked straight back in the opposite direction (including the steps). Each participant completed five laps. For the analysis of TGlittre, the best total time of two runs of the test was considered, and the result was compared with the reference values [31].

Statistical analysis

Data analysis was performed using IBM SPSS Statistics version 26.0 software (IBM Corp., Armonk, NY, USA). The normality of the variables was assessed using the Shapiro–Wilk test, and the results are expressed as measures of central tendency and dispersion appropriate for numerical data and frequency and percentage appropriate for categorical data. Comparisons between the measurements at baseline (T1) and those observed after 1 year (T2) were assessed using the Wilcoxon signed rank test. Comparisons of the changes (Δ) between the groups that did and did not engage in HPA (HPA group and NHPA group, respectively) were analyzed using the Mann–Whitney test. Comparisons of the changes between the groups who underwent or did not undergo CP (CP group and NCP group, respectively) were analyzed using the Mann–Whitney test. The relative changes were calculated as follows: $\Delta_{relative}$ (%) = (T2–T1)/T1 × 100. p≤0.05 was considered to indicate statistical significance.

Results

Among the 34 awCF who were evaluated for inclusion in the study, 10 were excluded for the following reasons: death during follow-up (n=4); exacerbation before evaluation (n=4); abandonment of CF treatment (n=1); and withdrawal from our center due to a change in residence (n=1). At baseline, the median age was 23 (19-27) years, with 17 (70.8%) males and 7 (29.2%) females. Fifteen (62.5%) and 10 (41.7%) participants engaged in HPA and CP, respectively. All awCF were receiving standard CF therapies. The mutations of the 24 awCF that were followed in the study are shown in Table 1.

The median body mass index (BMI) increased significantly from 19.8 (18-24) kg/m² at T1 to 21.4 (19-24) kg/m² at T2 (p=0.038). Muscle strength and pulmonary function did not significantly change between T1 and T2. Body composition, muscle strength, and pulmonary function were compared between T1 and T2, as shown in Table 2.

Regarding functional capacity during exercise, there was a significant reduction in the TGlittre time both in relation to absolute values [3.10 (2.52-3.39) *vs*. 2.40 (2.00-3.00) minutes, p=0.001] and in relation to the predicted values for the Brazilian population [31]: 127 (116-150) *vs*. 108 (102-140) % predicted, p=0.001. Although there was no significant increase in the 6MWD compared to the predicted values, it increased significantly compared to the absolute values [545 (463-654) *vs*. 617 (540-658) m, p=0.041). No changes were observed for the QoL assessed by the CFQ-R between T1 and T2, except for an increasing trend in the "treatment burden" domain of the CFQ-R (p=0.056). The compar-

Table 1. Mutations of the 24 adults with cystic fibrosis followed in the study.

1	F508del/F508del
2	F508del/F508del
3	F508del/F508del
4	F508del/G542X
5	F508del/G542X
6	F508del/3120+1G>A
7	F508del/3120+1G>A
8	F508del/232del18
9	F508del/V232D
10	F508del/G85E
11	F508del/2942insT
12	F508del/Y1092X
13	R334W/G85E
14	R334W/G542X
15	R334W/G542X
16	3120+1G>A/N
17	3120+1G>A/L206W
18	S549R/L206W
19	R1066C/D614G
20	G542X/N
21	G85E/G85E
22	G85E/p.Ser168Leu
23	Y1014C/W1282X
24	R1158X/G85E

Table 2. Comparisons between measurements of body composition, muscle strength, and lung function between baseline (T1) and 1 year later (T2).

Variable	T1	T2	p
BMI (kg/m²)	19.8 (18-24)	21.4 (19-24)	**0.038**
Muscle strength			
MIP (cm H_2O)	90 (71-108)	100 (73-118)	0.33
MEP (cm H_2O)	88 (71-100)	100 (80-100)	0.58
HGS (kgf)	36 (30-40)	38 (30-42)	0.22
Spirometry			
FVC (% predicted)	73 (59-83)	71 (49-81)	0.085
FEV_1 (% predicted)	57 (40-71)	53 (35-71)	0.078
FEV_1/FVC (%)	77 (65-85)	75 (66-91)	0.41

BMI, body mass index; MIP, maximal inspiratory pressure; MEP, maximal expiratory pressure; HGS, handgrip strength; FVC, forced vital capacity; FEV_1, forced expiratory volume in 1 second. The values shown are the mean ± standard deviation. Bold type indicates significant differences.

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isons between the measures of functional capacity during exercise and QoL between T1 and T2 are shown in Table 3.

When the groups who did and did not engage in HPA were compared, there was a significant difference in $\Delta HGS_{relative}$ between T1 and T2 [7.1 (0-20) kgf for the HPA group *vs*. 0 (-12-3) kgf for the NHPA group, p=0.031] (Figure 1). No other variables differed between the HPA and NHPA groups. When the groups that did and did not undergo CP were compared, there was a significant difference in the $\Delta_{relative}$ of the "treatment burden" domain of the CFQ-R between T1 and T2 [16.1 (-3-18) points for the CP group *vs*. -11.2 (-28-1) points for the NCP group, p=0.049] (Figure 2). No other variables differed between the CP and NCP groups.

Discussion

Tracking multiple outcome measures may provide a better and more complete picture to aid in clinical decision-making in individuals with CF. In the search for such outcome measures, we found that awCF experienced significant improvements in the

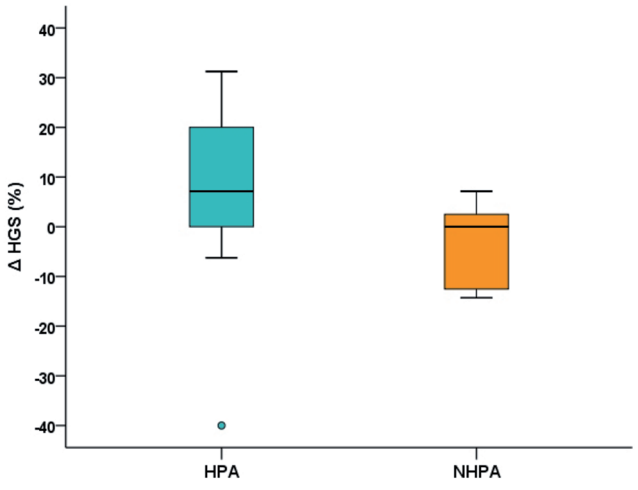

Figure 1. Relative delta of handgrip strength (HGS) between baseline (T1) and 1 year later (T2). A significant difference was identified between T1 and T2 when comparing the group that engaged in habitual physical activity (HPA) with the group that did not engage in HPA (NHPA) (p=0.031).

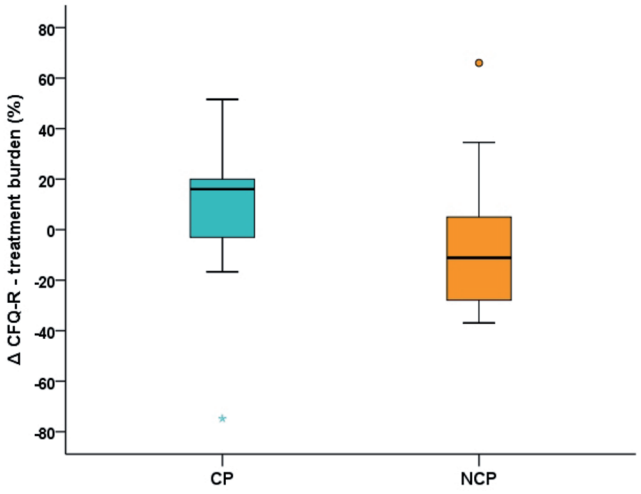

Figure 2. Relative delta of the "treatment burden" domain of the Cystic Fibrosis Questionnaire-Revised (CFQ-R) between baseline (T1) and 1 year later (T2). A significant difference was identified between T1 and T2 when comparing the group that underwent chest physiotherapy (CP) with the group that did not undergo CP (NCP) (p=0.049).

Table 3. Comparisons between measures of exercise functional capacity and quality of life between the beginning of the study (T1) and 1 year later (T2).

Variable	T1	T2	p
Functional capacity			
TGlittre time (min)	3.10 (2.52-3.39)	2.40 (2.00-3.00)	**0.001**
TGlittre time (% predicted)	127 (116-150)	108 (102-140)	**0.001**
6MWD (m)	545 (463-654)	617 (540-658)	**0.041**
6MWD (% predicted)	85 (74-98)	93 (85-98)	0.12
CFQ-R			
Physical functioning (points)	79 (56-91)	81 (51-96)	0.61
Role (points)	91 (75-100)	92 (75-100)	0.84
Vitality (points)	66 (58-81)	75 (58-87)	0.079
Emotional functioning (points)	83 (62-86)	80 (62-89)	0.91
Social functioning (points)	61 (55-76)	67 (51-83)	0.38
Body image(points)	66 (33-88)	78 (44-89)	0.093
Eating (points)	100 (77-100)	100 (77-100)	0.78
Treatment burden (points)	66 (58-85)	67 (55-78)	0.96
Health perceptions (points)	77 (55-88)	67 (56-97)	0.43
Weight (points)	66 (33-66)	67 (44-100)	0.056
Respiratory symptoms (points)	72 (50-87)	69 (57-95)	0.20
Digestive symptoms (points)	88 (77-97)	89 (78-100)	0.48

TGlittre, Glittre-activities of daily living test; 6MWD, 6-minute walking distance; CFQ-R, Cystic Fibrosis Questionnaire-Revised. The values shown are the mean ± standard deviation. Bold type indicates significant differences.

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TGlittre time and, to a lesser extent, the 6MWD, at the 1-year follow-up. These patients experienced an increase in BMI during the first year of this study. Furthermore, HPA seemed to positively impact peripheral muscle strength, while CP seemed to positively impact QoL, especially regarding the perception of treatment load.

The respiratory muscles of individuals with CF can be affected by several mechanisms, including lung hyperinflation, lack of HPA, systemic inflammation and even CFTR channel dysfunction [32]. FEV_1 is considered one of the best measures available for evaluating lung disease in CF patients and is an influential metric for defining the stage of the disease [33]. We did not observe any significant changes in lung function (including FEV_1) or respiratory muscle strength between T1 and T2. Evaluating European data between 2011 and 2021, Kerem *et al.* [33] observed a consistent improvement in FEV_1 and survival among 47,621 individuals with CF. The mean FEV_1 ranged from 63.6% to 74.7% in adults. Interestingly, FEV_1 increased even more among those carrying the F508del mutation in 2021, when HEMT was available. However, these authors observed that individuals with CF living in lower-income European countries did not demonstrate a significant annual increase in FEV_1. This at least partially explains our results, as they were collected from a center located in a country with scarce resources.

Several studies have shown that self-reported HPA and CP correlate with slower annual rates of decline in FEV_1 [19,34]. Contrary to these findings, we did not observe significant differences in lung function between the HPA and NHPA groups. Interestingly, we observed an increase in HGS between T1 and T2 in the HPA group but not in the NHPA group, reinforcing the importance of HPA as a contributor to the acquisition of greater skeletal muscle strength in patients who undergo CF [7]. Since HGS is a clinical marker of physical performance and all-cause mortality [35], HPA should be promoted in individuals with CF, even if HEMT is available and hypothetical new therapies come to market beyond those directed toward the F508del allele. In addition to pulmonary function being able to affect adherence to HPA in individuals with CF, numerous factors may support or prevent participation in HPA, including the degree of motivation, severity of the disease, presence of symptoms such as pain and dyspnea, individual confidence in one's ability to engage in exercise, accessibility to training sites, education level, and type of occupation [18].

Individuals with CF require tests that assess physical performance with lower energy expenditure; these tests should be easy to perform and appropriate for routine use in clinical practice, which are characteristics that are covered by submaximal exercise tests [36]. Although we did not observe a significant increase in the 6MWD between T1 and T2 relative to the predicted value, we detected a significant increase in the 6MWD relative to the absolute value. Considering the median 6MWD between T1 and T2, the increase in the 6MWD was well above the minimal clinically important difference of 33 m observed by Bhatia *et al.* [37] in a cohort of individuals with CF evaluated prospectively at 1-year intervals. The 6MWT provides important prognostic information for awCF, as a reduced 6MWT is associated with a greater need for LTX and a greater risk of death [6]. Although the 6MWT cannot replace pulmonary function tests, it may represent a valuable tool to expand the evaluation of therapeutic response in awCF. Since the correlation between the 6MWD and pulmonary function is weak [37], these two tools should be used as complementary tools in the longitudinal evaluation of individuals with CF.

A decrease in functional capacity during exercise has a negative impact on the prognosis of CF, so we should search for field tests that more reliably reflect the evolution of CF than the 6MWT [38]. The present study showed that the TGlittre could capture a greater change between T1 and T2 than the 6MWT could, possibly because the former requires the subject to perform multiple tasks, such as sitting, standing, walking, going up and down stairs, reaching and grabbing objects with their hands, transferring weights, and squatting [12]. In agreement with these findings, our group previously showed in a cross-sectional study that although awCF took longer to perform TGlittre than control participants did, no difference between these two groups was observed in the 6MWD [7]. Notably, intolerance to submaximal tests in individuals with CF is multifactorial and depends to a greater or lesser extent on pulmonary function, peripheral muscle function, the degree of systemic inflammation, the level of oxidative stress, nutritional status, the type of bronchial colonization, and the degree of HPA [36,39].

Another domain that has gained attention in protocols designed for awCF is QoL because, with the worsening of the disease, symptoms related to exercise intolerance can be triggered by decreasing physical effort, causing a decrease in QoL [40]. In our study, however, no change was observed in QoL between T1 and T2, except for an increasing trend in the "treatment burden" domain of the CFQ-R, which can be explained by the increase in BMI after 1 year. Interestingly, a study conducted by our group almost a decade ago [41] showed much lower scores in almost all the CFQ-R domains, which reflects the impact of treatment advancement in this period, even before HEMT. We also detected a positive impact of CP on the "treatment burden" domain of the CFQ-R between T1 and T2, in line with Kenn *et al.* [42], who showed that CP improves the QoL of awCF awaiting LTX.

For purposes of comparison with other real-life cohorts, our results may be useful for the follow-up of awCF, as they are already applicable to those who are not eligible (by genotype) for the use of HEMT and to the substantial proportion of awCF who live in countries where HEMT is not available. In Brazil, government regulation has recently established the following criteria for initiating HEMT in individuals with CF [43]: age 6 years or older and at least one F508del mutation in the CFTR dysfunction. This government regulation describes access to care, authorization, registration, and reimbursement of the corresponding procedures. Therefore, according to Table 1, 50% of our sample is eligible for immediate initiation of HEMT.

The strength of this study is that multiple outcome measures, including two tests of functional capacity on exertion, were evaluated in awCF over 1 year. However, some limitations should be noted. First, the study evaluated a small number of patients from a single CF center, although it had many data points because the patients were followed up for 1 full year. Second, we did not use the CPET to assess functional capacity during exercise, although it requires expensive and specific equipment for performance and specialized personnel and does not represent the usual HPA level of awCF [37]. Third, our results may not be applicable to awCF who have already undergone HEMT. The long-term impact of HEMT on disease progression and on the criteria for referral and listing of LTX has yet to be determined. Despite these limitations, our findings may serve as a guide for the monitoring of awCF both in clinical practice and in clinical trials to evaluate the efficacy of new drugs and/or rehabilitative strategies.

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Conclusions

In awCF, field tests are good tools for detecting longitudinal changes in health and QoL, although these individuals perform better in the TGlittre than in the 6MWT. Even without HEMT, there was a progressive increase in the BMI of awCF within 1 year. Furthermore, there was an interrelationship between HPA and peripheral muscle strength and between CP and QoL. The disparity between multiple outcome measures highlights that these measures together can provide a more complete picture of CF than any measure alone. Thus, our results may serve as a starting point for future studies in awCF cohorts undergoing HEMT to evaluate changes in submaximal field tests over time, including studies evaluating the long-term prognostic value of these tests.

References

1. Giallongo A, Parisi GF, Papale M, et al. Effects of elexacaftor/tezacaftor/ivacaftor on cardiorespiratory polygraphy parameters and respiratory muscle strength in cystic fibrosis patients with severe lung disease. Genes 2023;14:449.
2. Cutting GR. Cystic fibrosis genetics: from molecular understanding to clinical application. Nat Rev Genet 2015;16:45-56.
3. Gramegna A, Contarini M, Aliberti S, et al. From ivacaftor to triple combination: a systematic review of efficacy and safety of CFTR modulators in people with cystic fibrosis. Int J Mol Sci 2020;21:5882.
4. da Silva Filho LVRF, Maróstica PJC, Athanazio RA, et al. Extensive CFTR sequencing through NGS in Brazilian individuals with cystic fibrosis: unravelling regional discrepancies in the country. J Cyst Fibros 2021;20:473-84.
5. Sanders DB, Chmiel JF. Drug development for cystic fibrosis. Pediatr Pulmonol 2021:56:S10-22.
6. Martin C, Chapron J, Hubert D, et al. Prognostic value of six minute walk test in cystic fibrosis adults. Respir Med 2013; 107:1881-7.
7. Abelenda VLB, da Costa CH, Firmida MC, Lopes AJ. Evaluating the contribution of the Glittre-ADL test in adults with cystic fibrosis. Physiother Res Int 2024;29:e2087.
8. Papathanasiou J, Dionyssiotis Y, Kasnakova P, et al. Six-minute walk test: a tool for assessing mobility in frail subjects. J Frailty Sarcopenia Falls 2016;1:73-6.
9. Ramos KJ, Smith PJ, McKone EF, et al. Lung transplant referral for individuals with cystic fibrosis: Cystic Fibrosis Foundation consensus guidelines. J Cyst Fibros 2019;18:321-33.
10. Gur M, Masarweh K, Toukan Y, et al. Six-minute walk, lung clearance index, and QOL in bronchiolitis obliterans and cystic fibrosis. Pediatr Pulmonol 2019;54:451-6.
11. Combret Y, Boujibar F, Gennari C, et al. Measurement properties of the one-minute sit-to-stand test in children and adolescents with cystic fibrosis: a multicenter randomized cross-over trial. PLoS One 2021;16:e0246781.
12. Dourado VZ, Nishiaka RK, Simões MSMP, et al. Classification of cardiorespiratory fitness using the six-minute walk test in adults: comparison with cardiopulmonary exercise testing. Pulmonology 2021;27:500-8.
13. Frost AE, Langleben D, Oudiz R, et al. The 6-min walk test (6MW) as an efficacy endpoint in pulmonary arterial hypertension clinical trials: demonstration of a ceiling effect. Vascul Pharmacol 2005;43:36-9.
14. Skumlien S, Hagelund T, Bjørtuft O, Ryg MS. A field test of functional status as performance of activities of daily living in COPD patients. Respir Med 2006;100:316-23.
15. Scalco JV, Martins R, Almeida ACS, Caputo F, et al. "Test-retest reliability and minimal detectable change in TGlittre-P test in children and adolescents with cystic fibrosis". Disabil Rehabil 2022;44:3701-7.
16. de Andrade Junior AB, Ferreira AS, Assis ACB, et al. Cardiac autonomic control in women with rheumatoid arthritis during the glittre activities of daily living test. Asian J Sports Med 2020;11:e101400.
17. Balata MR, Ferreira AS, da Silva Sousa A, et al. Assessment of functional capacity in patients with nondialysis-dependent chronic kidney disease with the Glittre activities of daily living test. Healthcare 2023;11:1809.
18. Gruber W, Stehling F, Blosch C, et al. Longitudinal changes in habitual physical activity in adult people with cystic fibrosis in the presence or absence of treatment with elexacaftor/tezacaftor/ivacaftor. Front Sports Act Living 2024:6:1284878.
19. Southern KW, Addy C, Bell SC, et al. Standards for the care of people with cystic fibrosis; establishing and maintaining health. J Cyst Fibros 2024;23:12-28.
20. Gruet M, Saynor ZL, Urquhart DS, Radtke T. Rethinking physical exercise training in the modern era of cystic fibrosis: a step towards optimising short-term efficacy and long-term engagement. J Cyst Fibros 2022;21:e83-98.
21. Hamedi N, Kajbafvala M, ShahAli S, et al. The effects of aerobic exercises compared to conventional chest physiotherapy on pulmonary function, functional capacity, sputum culture, and quality of life in children and adolescents with cystic fibrosis: a study protocol for randomized controlled trial study. Trials 2023;24:695.
22. Farrell PM, White TB, Ren CL, et al. Diagnosis of cystic fibrosis: consensus guidelines from the Cystic Fibrosis Foundation. J Pediatr 2017:181S:S4-15.
23. McIlwaine M, Button B, Dwan K. Positive expiratory pressure physiotherapy for airway clearance in people with cystic fibrosis. Cochrane Database Syst Rev 2015;6:CD003147.
24. Rozov T, Cunha MT, Nascimento O, et al. Linguistic validation of cystic fibrosis quality of life questionnaires. J Pediatr 2006;82:151-6.
25. Crosby CA, Wehbe MA, Mawr, B. Hand strength: normative values. J Hand Surg Am 1994;19:665-70.
26. Culver BH, Graham BL, Coates AL, et al. Recommendations for a standardized pulmonary function report: an official American Thoracic Society technical statement. Am J Respir Crit Care Med 2017;196:1463-72.
27. Pereira CA, Sato T, Rodrigues SC. New reference values for forced spirometry in white adults in Brazil. J Bras Pneumol 2007;33:397-406.
28. American Thoracic Society/European Respiratory Society. ATS/ERS statement on respiratory muscle testing. Am J Respir Crit Care Med 2002;166:518-624.
29. ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories. ATS statement: guidelines for the six-minute walk test. Am J Respir Crit Care Med 2002; 166:111-7.
30. Enright PL, Sherrill DL. Reference equations for the six-minute walk in healthy adults. Am J Respir Crit Care Med 1998;158:1384-7.
31. Reis CMD, Karloh M, Fonseca FR, et al. Functional capacity

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measurement: reference equations for the Glittre Activities of Daily Living test. J Bras Pneumol 2018;44:370-7.
32. Gusev E, Liang F, Bhattarai S, et al. Characterization of skeletal muscle wasting pathways in diaphragm and limb muscles of cystic fibrosis mice. Am J Physiol Regul Integr Comp Physiol 2022;322:R551-61.
33. Kerem E, Orenti A, Adamoli A, et al. Cystic fibrosis in Europe: improved lung function and longevity - reasons for cautious optimism, but challenges remain. Eur Respir J 2024;63: 2301241.
34. Boutou AK, Manika K, Hajimitrova M, et al. Longitudinal changes in exercise capacity among adult cystic fibrosis patients. Adv Respir Med 2020;88:420-3.
35. Lima TRL, Almeida VP, Ferreira AS, et al. Handgrip strength and pulmonary disease in the elderly: what is the link? Aging Dis 2019;10:1109-29.
36. Andrade Lima C, Dornelas de Andrade A, et al. Six-minute walk test as a determinant of the functional capacity of children and adolescents with cystic fibrosis: a systematic review. Respir Med 2018:137:83-8.
37. Bhatia R, Kaye M, Roberti-Miller A. Longitudinal assessment of exercise capacity and quality of life outcome measures in cystic fibrosis: a year-long prospective pilot study. J Eval Clin Pract 2020;26:236-41.
38. Campos NE, Vendrusculo FM, Da Costa GA, et al. The association of field test outcomes with peak oxygen uptake in patients with cystic fibrosis: a systematic review. Int J Exerc Sci 2022;15:1381-94.
39. Bradley J, McAlister O, Elborn S. Pulmonary function, inflammation, exercise capacity and quality of life in cystic fibrosis. Eur Respir J 2001;17:712-5.
40. Cherobin IA, Dalcin PTR, Ziegler B. Association between lung function, physical activity level and postural evaluation variables in adult patients with cystic fibrosis. Clin Respir J 2018;12:1510-7.
41. Ribeiro Moço VJ, Lopes AJ, dos Santos Vigário P, et al. Pulmonary function, functional capacity and quality of life in adults with cystic fibrosis. Rev Port Pneumol 2015;21:198-202.
42. Kenn K, Gloeckl R, Soennichsen A, et al. Predictors of success for pulmonary rehabilitation in patients awaiting lung transplantation. Transplantation 2015;99:1072-7.
43. Ministry of Health of Brazil. Approves the clinical protocol and therapeutic guidelines for cystic fibrosis, 30 April 2024. Available from: https://www.gov.br/saude/pt-br/assuntos/pcdt/arquivos/2022/portal-portaria-conjunta-no-25_pcdt_fibrose-cistica.pdf/view

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