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**TEST-RETEST RELIABILITY, MINIMAL DETECTABLE CHANGE AND  
MINIMAL CLINICALLY IMPORTANT DIFFERENCES IN MODIFIED  
SHUTTLE WALK TEST IN CHILDREN AND ADOLESCENTS WITH CYSTIC  
FIBROSIS**

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The study protocol was approved by the local Ethics Committee of the Center for  
Advanced Studies University La Salle (Madrid, Spain; N°: PI-169/2017). All  
participants gave written informed consent before data collection began.

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Abbreviated Title: Modified-shuttle walk test in cystic fibrosis children

## ABSTRACT

*Background:* In youths with cystic fibrosis (CF) the modified shuttle walk test (MSWT) has been shown to be useful for assessing exercise tolerance; however, no studies to date have evaluated the reliability of MSWT, the minimal detectable change (MDC) and the minimal clinically important differences (MCID) for the MSWT distance for children and adolescents with CF.

*Methods:* Test-retest reliability: 35 CF patients and 34 healthy controls performed two MSWTs (separated by 2–4 days). MCID: 33 patients were invited to participate in a 6-week home-based exercise program consisting of 30 to 60-min sessions, 5 days a week.

*Results:* The test-retest reliability of the MSWT distance for children and adolescents with CF was excellent, obtaining a MDC<sub>90</sub> and MDC<sub>95</sub> of 97.08m and 115.32m, respectively. The test-retest reliability also was excellent in healthy controls, founding a MDC<sub>90</sub> and MDC<sub>95</sub> of 69.12m and 82.11m, respectively. The ROC curve analysis established (with a sensitivity of 82% and specificity of 76%) that a change of 60 m represented MCID.

*Conclusions:* The MSWT is a reliable tool to measure of exercise tolerance in children/adolescents with CF and those without CF. We propose a change in the score of at least 97.08 m (MDC<sub>90</sub>) as the most appropriate value for assessing the exercise response of children and adolescents with CF, given that this value exceeds the MCID based on the children's perception.

*Keywords:* cystic fibrosis; shuttle walk test; submaximal exercise testing; pulmonary rehabilitation; physical activity; children and adolescents.

*Abbreviators:* CF, cystic fibrosis; MSWT, modified shuttle walk test; MDC, minimal detectable change and MCID, minimal clinically important difference.

## 1. Introduction

Exercise capacity in patients with cystic fibrosis (CF) is limited by cardiorespiratory and metabolic determinants, with contributing factors including muscle mass, muscle function (peripheral skeletal or respiratory), progressive respiratory disease and systematic inflammation [1,2]. Exercise tolerance is also positively and longitudinally associated with health-related quality of life [3] and survival [4] in these patients.

Children with CF with higher activity levels have been shown to have better aerobic and anaerobic capacity, improved nutritional status and significantly lower disease severity [5–7]. Due to each patient’s differing characteristics, the significant impact of exercise on quality of life and its prognostic value, detailed exercise testing is required before starting exercise training to provide safe and effective training recommendations to patients with CF.

In terms of validity, precision and objectivity, cardiopulmonary exercise testing (CPET) is considered the gold standard for assessing functional capacity and limitations.

However, CPET requires expensive laboratory equipment and expert staff and is unavailable to many CF clinicians. Given time constraints, a lack of staff, funding and sophisticated equipment, simple field exercise testing might be the preferred method for evaluating exercise tolerance (e.g., the distance a patient can walk or run), estimating peak aerobic capacity and determining the effects of therapeutic interventions. The 20-m shuttle run test and the 10-m shuttle walk are incremental, externally paced exercise tests that are well-tolerated, reliable and valid for children with CF [8]. However, the 20-m shuttle run test might prove too taxing for children, and the 10-m shuttle walk test would show a ceiling effect when the maximum distance of 1500 m is reached. We therefore suggest the modified version of the 10-m shuttle walk test (MSWT) by adding

1 three levels and allowing patients to run, thus allowing them to reach maximum  
2 exercise capacity. Studies have shown that MSWT is reliable and valid for assessing  
3 exercise tolerance in adults with CF [9,10] and is better at detecting oxygen desaturation  
4 and carbon dioxide retention than CPET in this population [11]. For younger patients  
5 with CF, MSWT has been shown to be useful in determining clinical improvement after  
6 hospitalization [12]. However, no studies to date have evaluated the reliability of  
7 MSWT in children and adolescents with CF.  
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18 When working with patients with reduced exercise capacity, it is important to know  
19 whether the clinically meaningful changes in exercise capacity are related to the  
20 therapeutic interventions. Ascertaining what constitutes a clinically significant  
21 improvement in exercise capacity is therefore essential. The minimal detectable change  
22 (MDC) is defined as the smallest change in score that can be detected beyond random  
23 error [13]. Another option for identifying interventions that help increase exercise  
24 tolerance is to determine the minimal clinically important difference (MCID): the  
25 smallest change in an outcome measure that is recognized by the patient as beneficial  
26 [14]. To our knowledge, no MDC or MCID has yet been defined for MSWT for  
27 children and adolescents with CF. Thus, the primary aim of this study was to provide  
28 test-retest reliability and to establish the MDC for the MSWT distance for children and  
29 adolescents with CF. Our secondary aim was to determine the MCID for the MSWT  
30 distance for children and adolescents with CF. Finally, the third aim was to compare the  
31 MSWT distance and the muscular strength in the upper/lower extremities between  
32 children/adolescents with CF and those without CF.  
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## 2. Materials and methods

### 2.1 Study design

For this study, the researchers performed three different assessments: (1) a repeated measures concordance design was used to assess the test-retest reliability of the MSWT distance (comparing performance on two separate days) for children and adolescents with stable CF; (2) a quantitative quasi-experimental design study to establish the MCID for the MSWT distance in the same population; and (3) a cross-sectional study to detect differences in exercise tolerance and strength between participants with CF and healthy controls. The protocol was approved by the Ethics Committee of the La Salle University Center for Advanced Studies (Madrid, Spain) (registration number: CSEULS-PI-169/2017) and was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all the children and from their parents or legal guardians. To calculate the sample size to assess the test-retest reliability and to detect differences in exercise tolerance and strength, we chose a power of 90%, a significance level of 5% and a large effect size ( $d=0.8$ ), based on a similar study performed on this population [15]. Thus, a total sample size of at least 68 participants was required. To establish the MCID, at least 22 patients were required to obtain a 95% confidence level and a margin of error of 3% (precision) for the results, considering that the percentage of the Spanish population with this disease is less than 0.5% [16]. Hence, a sample of 34 participants per group was ultimately established.

### 2.2 Study population

Children and adolescents (7 to 17 years) with CF were recruited from the Cystic Fibrosis Association of Madrid, and healthy controls (7 to 17 years) were recruited from a local sports center (Centro Deportivo Unión Aravaca), via bulletin advertisements by

1 e-mail and flyer distribution, using convenience sampling in both cases. All patients  
2 were clinically stable, had been familiarized with the exercise test and were undergoing  
3 routine patient management. The healthy control group consisted of children and  
4 adolescents with no history of pulmonary, cardiovascular, neuromuscular or  
5 osteoarticular comorbidities that would limit their participation in exercise tolerance  
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## 16 *2.3 Outcomes*

### 17 *2.3.1 Spirometry*

18 Spirometry was assessed with a portable spirometer (Spirobank II USB<sup>®</sup>, MIR, Rome,  
19 Italy) according to the American Thoracic Society/European Respiratory Society  
20 guidelines for the standardization of spirometry [17].  
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### 29 *2.3.2 Exercise test: modified version of the 10-m shuttle walk test*

30 For the MSWT, participants sat quietly on a chair for 10 minutes while their resting  
31 oxygen saturation and resting heart rate were measured with a WristOx2<sup>®</sup> Model 3150  
32 pulse oximeter. The participants' perceived breathlessness and subjective fatigue in the  
33 legs were assessed with the modified Borg scale [18]. The participants then underwent  
34 the 15-level MSWT, where they walked or ran repeatedly from one end of a 10-m  
35 corridor to the other. The corridor was marked with cones, and the participants had to  
36 increase their speed every minute, as dictated by an external audio signal [9,10]. The  
37 physiotherapist accompanied the participants during the first minute of the test. The end  
38 point of the test was determined either by the patient becoming too breathless to  
39 maintain the pace or by the physiotherapist when the participant was no longer able to  
40 complete a shuttle in the time allowed [19]. The measurements included the distance  
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1 walked/ran, the oxygen saturation and heart rate at the end of the test, and the peak  
2 rating of perceived breathlessness and subjective fatigue in the legs.  
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5 All participants made two visits (separated by 2–4 days) to the research laboratory of  
6 the La Salle University Center for Advanced Studies, during which they completed two  
7 MSWTs with a 20–30-min rest between tests. Test-retest reliability and MDC were  
8 assessed using the MSWT distance measured during the two visits, and the  
9 measurements performed during the second visit were employed to compare exercise  
10 tolerance and strength in the upper/lower extremities between the children/adolescents  
11 with CF and those without CF. The second visit measurements were chosen to increase  
12 participants' familiarization with the tests.  
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### 26 *2.3.3 Muscular strength tests*

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30 To test the participants' isometric hand and forearm strength, we employed a hand  
31 dynamometer device (JAMAR<sup>®</sup>, Patterson Medical, IL, USA) [20]. Three separate tests  
32 were administered for the right and left hands, and the highest value (kg) was recorded.  
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34 The medicine ball throw test was used to assess explosive arm power [21]. Participants  
35 held the ball behind their heads and then threw the ball forward vigorously; the farthest  
36 throw was recorded. To measure explosive leg power, the participants performed the  
37 horizontal jump test [22] by leaping horizontally as far as possible; the farthest distance  
38 was recorded. The measurements performed during the second visit were employed to  
39 compare exercise tolerance and strength in the upper/lower extremities between the  
40 children/adolescents with CF and those without CF.  
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### 54 *2.4 Minimal Detectable Change and Minimal Clinically Important Difference*

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1 The MDC was assessed using the MSWT distance measured during the two visits  
2 (separated by 2–4 days). The MDC was calculated using the standard error of  
3 measurement (SEM). The SEM can also be used to measure the degree of variability  
4 (confidence interval) of a participant's score that is not attributable to the true changes  
5 [23]. The SEM was calculated as:  $DS \times \sqrt{1 - ICC}$  (intraclass correlation coefficient),  
6 and it was also used to calculate the MDC as a 90% and 95% of the confidence  
7 interval:  $MCD_{90} = SEM \times \sqrt{2} \times 1.65$ , and  $MCD_{95} = SEM \times \sqrt{2} \times 1.96$ ,  
8 respectively.  
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21 After the second visit, only the patients were invited to participate in a 6-week home-  
22 based exercise program consisting of 30 to 60-min sessions, 5 days a week (including  
23 aerobic activities and resistance exercises), based on the results of a previous study on  
24 children and adolescents with CF [24]. This program was performed using a Nintendo  
25 Wii™ platform with the game EA SPORTS™ ACTIVE 2. At the beginning of each  
26 week, the video game included a maximum heart rate test to help patients to control  
27 their heart rate evolution and monitor daily exercise intensity. The training load was  
28 increased every week in order to perform all activities at 70-80% maximal heart rate.  
29 All exercise activities were adjusted according to age and patient preferences to  
30 improve motivation among the children/adolescents. A physiotherapist supervised the  
31 first session to ensure that the patients performed the exercises correctly. The  
32 physiotherapist also provided weekly telephone check-ins to increase patient adherence  
33 and parents supervised the remaining training sessions. Patients had to perform at least  
34 80% of the training sessions in order not to be eliminated from the study.  
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56 At the end of the exercise program, only the patients made a third visit (postprogram  
57 assessment) during which they completed two MSWTs with a 20–30-min rest between  
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1 tests. During the postprogram assessment and immediately after completing the test, the  
2 patients were asked to rate the change they felt in their exercise tolerance by answering  
3 the following question: “*Compared with the last time, how would you rate your exercise*  
4 *tolerance?*” Responses were categorized on a 5-point scale: (1) significantly better, (2)  
5 slightly better, (3) unchanged, (4) slightly worse and (5) significantly worse. The MCID  
6 was only calculated for symptomatic participants because it considered a measure of  
7 clinical improvement and because asymptomatic participants might have a ceiling  
8 effect.  
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## 10 11 12 13 14 15 16 17 18 19 20 21 *2.5 Statistical analysis*

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24 The data analysis was performed using SPSS version 21.0 (SPSS Inc., Chicago, IL,  
25 USA). For all analyses, the statistical significance was set at 5% ( $p < .05$ ). We employed  
26 the ICC by a 2-way fixed-effect model to evaluate the test-retest reliability of the  
27 distance obtained in the MSWT. Reliability levels were defined based on the following  
28 classification: excellent reliability ( $ICC \geq 0.90$ ), good reliability ( $0.90 > ICC \geq 0.70$ ), fair  
29 reliability ( $0.70 > ICC \geq 0.40$ ) and poor reliability ( $ICC < 0.40$ ) [25]. The SEM and the  
30 MDC were calculated following the same criteria as a previous study [26].  
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42 The MCID for participant perceived improvement was determined using anchor-based  
43 methods. The ROC curve analysis employed the change in the overall rating of the  
44 participant’s exercise tolerance as an external criterion (anchor) to determine the  
45 optimal cut-off value that corresponded to the least misclassification for discriminating  
46 between the participants who improved and the participants who were unchanged or  
47 poorer. Although changes in the overall rating were recorded using a 5-point scale, we  
48 employed a 3-point scale for the ROC curve analysis: (1) improved (including  
49 “significantly better” and “slightly better”), (2) unchanged and (3) poorer (including  
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1 “slightly worse” and “significantly worse”). Comparisons between groups were  
2 performed using nonparametric tests due to the fact that only 5 patients perceived their  
3 exercise tolerance as “slightly worse” or “significantly worse”. Specifically, the  
4 Kruskal-Wallis test was used to evaluate the group factor (three groups) at the onset of  
5 intervention. Post hoc intergroup comparisons for the change in the MSWT distance  
6 were examined using the U-Mann-Whitney test, while the Wilcoxon test was used to  
7 evaluate post hoc intragroup comparisons (pre-post intervention). Effect sizes between  
8 the groups were calculated according to Cohen’s method using the following categories:  
9 small (0.20–0.49), medium (0.50–0.79) or large ( $\geq 0.8$ ) [27]. For the distribution-based  
10 approach, the effect size method and the SEM method were employed [28].  
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25 We employed Student’s t-test to detect differences between the children/adolescents  
26 with CF and those without CF for exercise tolerance and strength.  
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### 33 **3. Results**

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37 The study sample consisted of a total of 68 participants; 35 children and adolescents  
38 with CF and 34 healthy controls. In general, the participants tolerated the tests well, and  
39 there were no significant differences between the groups in terms of anthropometric  
40 characteristics and lung function (**table 1**).  
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#### 48 *Assessment 1: Test-retest reliability of the MSWT distance*

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52 There were no differences in exercise performance between the two visits in any of the  
53 tests in either the patients with CF or the controls. The test-retest reliability of the  
54 distance measured during the MSWT was excellent, achieving values close to 1, which  
55 represented strong reliability in both participant groups. The SEM for the distance  
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1 measured for the MSWT was higher for the children/adolescents with CF than for the  
2 healthy controls. The MDC was therefore lower for the healthy controls than for the  
3 participants with CF. The descriptive statistics, ICCs and associated 95% CIs, SEMs,  
4 MDC<sub>90</sub> and MDC<sub>95</sub> are shown in **table 2**. **Figure 1** shows the Bland-Altman plots for  
5 the test-retest reliability of the MSWT distance for the patients with CF and the  
6 controls. **Supplemental table 1** shows descriptive statistics for all the tests in  
7 children/adolescents with CF and healthy controls.  
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18 *Assessment 2: Minimal clinically important difference of the MSWT distance*  
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21 Of the 35 patients with CF who were invited, 2 children did not complete the exercise  
22 program due to a lack of time, and another child withdrew due to pulmonary  
23 exacerbation. Thus, 33 patients with CF were analyzed. No adverse effects were  
24 reported during the training program (except for muscle stiffness), and the participants  
25 performed the test without incidents  
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29 The distribution of patient responses according to their exercise tolerance was  
30 “significantly better” in 27% (n = 9), “slightly better” in 9% (n = 3), “unchanged” in  
31 49% (n = 16), “slightly worse” in 9% (n = 3), and “significantly worse” in 6% (n = 2).  
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33 The Kruskal-Wallis test showed that there were no significant differences in baseline  
34 characteristics between the “improved”, “unchanged” and “poorer” groups. The change  
35 observed in the MSWT distance after the exercise program for the entire sample was  
36  $37.81 \pm 65.09$  m (baseline:  $899.69 \pm 266.44$  m; postintervention:  $937.5 \pm 254.14$  m).  
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39 The effect size for the entire sample change was 0.14; for the patients classified as  
40 improved, unchanged and poorer, the effect sizes were 0.32, 0.13 and 0.15, respectively.  
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1 with their changes in the MSWT distance —the better they perceived their exercise  
2 tolerance, the greater was the increase in the MSWT distance— (Rho = 0.580; p<.001).

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4 **Table 3** shows the descriptive statistics for the change in MSWT distance for the three  
5 response categories, as well as the multiple comparisons between them. **Supplemental**  
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9 **table 2** shows descriptive statistics for the rest of the exercise tolerance variables.

10 The ROC curve analysis established (with a sensitivity of 82% and specificity of 76%)  
11 that a change of 60 m represented clinically meaningful improvement. Assuming 60 m  
12 as the MCID, 18% of the patients who classified themselves as improved were therefore  
13 misclassified as unchanged. The analysis obtained an ROC value of 0.79 (95% CI,  
14 0.63–0.95; p=.008) (**Fig. 2**).

15  
16 Both distributed-based approaches (effect size method and SEM method) yielded an  
17 MCID to detect improvements in the MSWT of 53.29 m.

### 18 19 20 21 22 23 24 25 26 27 28 29 30 *Assessment 3: Exercise tolerance and strength*

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33 There were differences in terms of exercise tolerance and peripheral muscle strength  
34 between the patients with CF and the healthy controls, with better results for the healthy  
35 controls than for the patients with CF. End-of-test perceived dyspnoea and leg fatigue  
36 scores were significantly higher for the healthy controls than for the CF patients  
37 (p<.001). **Table 4** lists the mean shuttle distance completed, the peak rating of  
38 perceived breathlessness, the leg fatigue during the test and the strength in the  
39 extremities for both groups.  
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## 56 **4. Discussion**

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1 This study has shown that MSWT is reliable, yielding excellent results for children and  
2 adolescents with and without CF. Based on our results, MSWT can be applied with  
3 accuracy to children and adolescents with CF with well-preserved lung function. In  
4 terms of exercise tolerance and peripheral muscle strength, we obtained better results  
5 from the healthy controls than from the children and adolescents with CF. To our  
6 knowledge, this is the first study to assess the reliability of MSWT in this population.  
7 Previous studies have assessed the validity and reliability of MSWT for adults with CF  
8 and have shown its excellent reproducibility [9,10]. To assess test-retest reliability,  
9 Bradley et al. [10] employed correlation coefficients instead of the ICC. According to a  
10 number of authors, the ICC is a better measure of reliability that reflects both the degree  
11 of correlation and agreement between various estimates of the population measurements  
12 [29]. Moreover, the Pearson correlation coefficient does not detect systematic errors but  
13 rather hides them. Our study therefore employed the ICC. Compared with correlation  
14 coefficients, the ICC selection process is more appropriate and precise for evaluating  
15 test-retest reliability.  
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37 This study also reported the MDC, SEM and MCID for the distances in the MSWT  
38 achieved by children and adolescents with CF. Using the Bland and Altman plot method  
39 on adults with CF, Bradley et al. [10] reported that a change of at least 40 m was  
40 considered clinically significant. For our study, which employed the anchor-based  
41 approach to ascertain MCID, any change greater than 60 m was considered clinically  
42 significant. The variation observed between the 2 studies could be explained by the fact  
43 that the anchor-based approach is essentially based on the participant's perceived  
44 improvement after an intervention and is therefore subjective, unlike the method  
45 employed in Bradley's study, which was based on calculations and not on an  
46 intervention. In fact, our results using a distribution-based approach (53.29 m) were  
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1 more similar to those obtained in Bradley's study. In addition, the effect size in our  
2 study for the entire sample change was small (0.14) but was slightly larger for the  
3 patients classified as improved (0.32). This difference indicates that the MSWT might  
4 be able to discriminate small to moderate improvements and that there is still room for  
5 improvement in identifying the most effective intervention.  
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12 According to the MDC established in the present study through a distribution-based  
13 approach, children and adolescents with CF require a difference in the distance achieved  
14 during the MSWT of at least 97.08 m to consider it a real change (MDC<sub>90</sub> of 97.08 m  
15 and MDC<sub>95</sub> of 115.32 m). Although this method for calculating the MCD is similar to  
16 that employed by Bradley et al. [10] (both studies employed a distribution-based  
17 method, and the MSWT was performed on two occasions spaced a similar time apart  
18 and without applying any intervention between them), the difference between the two  
19 studies was paradoxically even greater. The reason for this difference could be due to  
20 two aspects. First, the method relying on SEM and MDC ensures the statistical  
21 soundness of the MCID value and represents a more conservative and exhaustive  
22 method [28], whereas the Bland and Altman plot method employed in the Bradley's  
23 study considers only the standard deviation and mean difference. Second, our study was  
24 conducted with children instead of adults; greater variability in our sample would  
25 therefore be expected. The numerous factors that could affect the variation in distance  
26 between the two visits for the children and adolescents with CF include fatigue, lack of  
27 motivation, boredom and lack of responsibility [30]. However, despite the greater  
28 variability, the test's reliability for this population was excellent.  
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55 As with other studies [15,31,32], our results showed a reduction in exercise tolerance  
56 and strength in the upper/lower extremities for the children and adolescents with CF  
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1 compared with the healthy controls, and these difference were large ( $d > 0.8$ ). However,  
2 the perceived breathlessness and subjective leg fatigue showed higher values in the  
3 healthy controls. These surprising results are supported by a previous report [31]. It is  
4 possible that, given the progressive nature of the disease, children with CF present  
5 adaptations to pulmonary impairment, do not perceive their limitations in terms of  
6 exercise tolerance and become accustomed to the perceived breathlessness.  
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15 The results of this study help us determine whether there have been real and clinical  
16 relevant changes in exercise tolerance (as measured by the MSWT) in children and  
17 adolescents with CF. It is therefore possible to determine whether patients present  
18 impaired physical capacity and identify the effectiveness of therapies aimed at  
19 alleviating or improving these aspects. In our opinion, the MDC established by this  
20 study would be a more appropriate value for assessing the response in terms of exercise  
21 tolerance by the MSWT, given that this value exceeds the MCID. The MCID  
22 calculation was performed to ensure that it would be a real change based on the  
23 participants' perception of improvement; however, numerous cognitive factors might  
24 influence the outcome due to the placebo effect. Therefore, and from an ethical point of  
25 view, the results obtained for the MDC would be a more appropriate value for the  
26 MCID.  
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46 The present study has a number of limitations, the primary being the fact that we did not  
47 use conventional CPET to asses exercise tolerance. However, the field test has been  
48 demonstrated to be reliable and valid for assessing the exercise tolerance of patients  
49 with CF [8–10,33–35]. Furthermore, 36% of the participants perceived their exercise  
50 tolerance as “slightly better” following the exercise program, whereas 49% judged that  
51 they did not improve. This finding could be influenced by the participants' subjective  
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1 assessment of their perceived improvement. However, the effect size obtained after the  
2 intervention was small. According to our results, there appears to be room for  
3 improvement in the intervention aimed at improving exercise tolerance. Finally, another  
4 limitation is that healthy controls did not perform the 6-week exercise program, so we  
5 could not made comparisons between groups after intervention, nor could establish the  
6 MCID for the asymptomatic population. However, the MCID for asymptomatic controls  
7 probably show a ceiling effect.  
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12 In conclusion, this study provided evidence of the reliability of the MSWT as a measure  
13 of exercise tolerance and established the MDC and MCID for the MSWT distance for  
14 children and adolescents with CF. We propose a change in the score of at least 97.08 m  
15 (MDC<sub>90</sub>) as the most appropriate value for assessing the exercise response of children  
16 and adolescents with CF, given that this value exceeds the MCID based on the  
17 children's perception. In addition, we found differences in the MSWT distance and  
18 strength in the upper/lower extremities between children/adolescents with CF and those  
19 without CF. However, these findings should be comforted by other studies due to the  
20 low number of participants and wide dispersion of age. Future studies solving these  
21 concerns are needed.  
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#### 45 **Acknowledgements**

46 The authors like to thank the parents and patients taking part in this study and the  
47 Asociación Madrileña contra la Fibrosis Quística for their help.  
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50  
51 The authors certify that they have no affiliations with or financial involvement in any  
52 organization or entity with a direct financial interest in the subject matter or materials  
53 discussed in the article.  
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This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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**Table 1.** Anthropometric characteristics and lung function for children and adolescents with cystic fibrosis (CF) and healthy controls. Data are presented as mean±SD.

|                                 | <b>Children/adolescents with<br/>CF (n=35)</b> | <b>Healthy controls<br/>(n=34)</b> |
|---------------------------------|--|------------------------------------|
| <b>Anthropometric variables</b> |  |                                    |
| <b>Age</b> (years)              | 11.54 ± 3.67                                   | 12.48 ± 3.07                       |
| <b>Gender</b> (female:male)     | 15:20  | 13:21                              |
| <b>Height</b> (cm)              | 145.94 ± 17.05                                 | 156.79 ± 20.11                     |
| <b>Weight</b> (Kg)              | 40.29 ± 14.33                                  | 48.26 ± 15.57                      |
| <b>Respiratory function</b>     |  |                                    |
| <b>FEV<sub>1</sub></b> (% pred) | 83.81 ± 23.73                                  | 98.88 ± 12.61                      |
| <b>FVC</b> (% pred)             | 93.47 ± 20.25                                  | 101.33 ± 14.28                     |
| <b>FEV<sub>1</sub>/FVC</b> (%)  | 76.64 ± 10.13                                  | 89.1 ± 6.03                        |

FEV<sub>1</sub>: forced expiratory volume at the first second; FVC: forced vital capacity.

**Table 2.** Descriptive statistics, intraclass correlation coefficient (ICC), associated 95% confidence interval (CI), standard error of measurement (SEM), minimal detectable change (MDC).

| <b>Children/adolescents with CF (2 days n=35)</b> |                 |                |                        |            |                         |                         |
|---|-----------------|----------------|------------------------|------------|-------------------------|-------------------------|
|   | <b>Mean±SD</b>  |                | <b>ICC (95% CI)</b>    | <b>SEM</b> | <b>MDC<sub>90</sub></b> | <b>MDC<sub>95</sub></b> |
|   | <b>Day 1</b>    | <b>Day 2</b>   |                        |            |                         |                         |
| <b>MSWT (m)</b>                                   | 849.14 ± 262.88 | 867.43 ± 276.2 | 0.975 (0.951 to 0.987) | 41.6       | 97.08                   | 115.32                  |

| <b>Healthy controls (2 days n=34)</b> |                  |                  |                        |            |                         |                         |
|---------------------------------------|------------------|------------------|------------------------|------------|-------------------------|-------------------------|
|                                       | <b>Mean±SD</b>   |                  | <b>ICC (95% CI)</b>    | <b>SEM</b> | <b>MDC<sub>90</sub></b> | <b>MDC<sub>95</sub></b> |
|                                       | <b>Day 1</b>     | <b>Day 2</b>     |                        |            |                         |                         |
| <b>MSWT (m)</b>                       | 1197.88 ± 278.15 | 1181.52 ± 284.16 | 0.988 (0.975 to 0.994) | 29.62      | 69.12                   | 82.11                   |

MSWT: modified shuttle walk test.

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**Table 3.** Descriptive statistics for change in exercise tolerance.

|                        | MSWT distance (m)<br>Pre-intervention                      | MSWT distance<br>(m) Post-<br>intervention | Change in MSWT<br>distance (m) | Wilcoxon test,<br>P-value<br>pre-post intervention |
|------------------------|--|--|--------------------------------|--|
| <b>Improved</b>        | <b>Median (1<sup>st</sup> and 3<sup>rd</sup> quartile)</b> |  |                                |  |
|                        | 850<br>(720 and 1170)                                      | 940<br>(820 and 1240)                      | 70<br>(70 and 100)             | 0.005  |
|                        | <b>Mean ± SD</b>   |  |                                |  |
|                        | 931.82 ± 257.41  | 1011.82 ± 245.47                           | 80 ± 43.13                     | -  |
| <b>Unchanged</b>       | <b>Median (1<sup>st</sup> and 3<sup>rd</sup> quartile)</b> |  |                                |  |
|                        | 735<br>(650 and 1037.5)                                    | 785<br>(697.5 and 1080)                    | 25<br>(0 and 80)               | 0.023  |
|                        | <b>Mean ± SD</b>   |  |                                |  |
|                        | 843.75 ± 262.09  | 878.13 ± 258.67                            | 34.38 ± 49.39                  | -  |
| <b>Poorer</b>          | <b>Median (1<sup>st</sup> and 3<sup>rd</sup> quartile)</b> |  |                                |  |
|                        | 990<br>(765 and 1260)                                      | 900<br>(755 and 1205)                      | -20<br>(-120 and 20)           | 0.273  |
|                        | <b>Mean ± SD</b>   |  |                                |  |
|                        | 1008 ± 311.32  | 964 ± 262.36                               | -44 ± 75.7                     | -  |
| <b>U- Mann-Whitney</b> |  |  |                                |  |
|                        | <b>a) Improved vs. Unchanged</b>                           |  | a) 0.041                       |  |
|                        | <b>b) Improved vs. Poorer</b>                              |  | b) 0.004                       |  |
|                        | <b>c) Unchanged vs. Poorer</b>                             |  | c) 0.033                       |  |

MSWT: modified shuttle walk test.

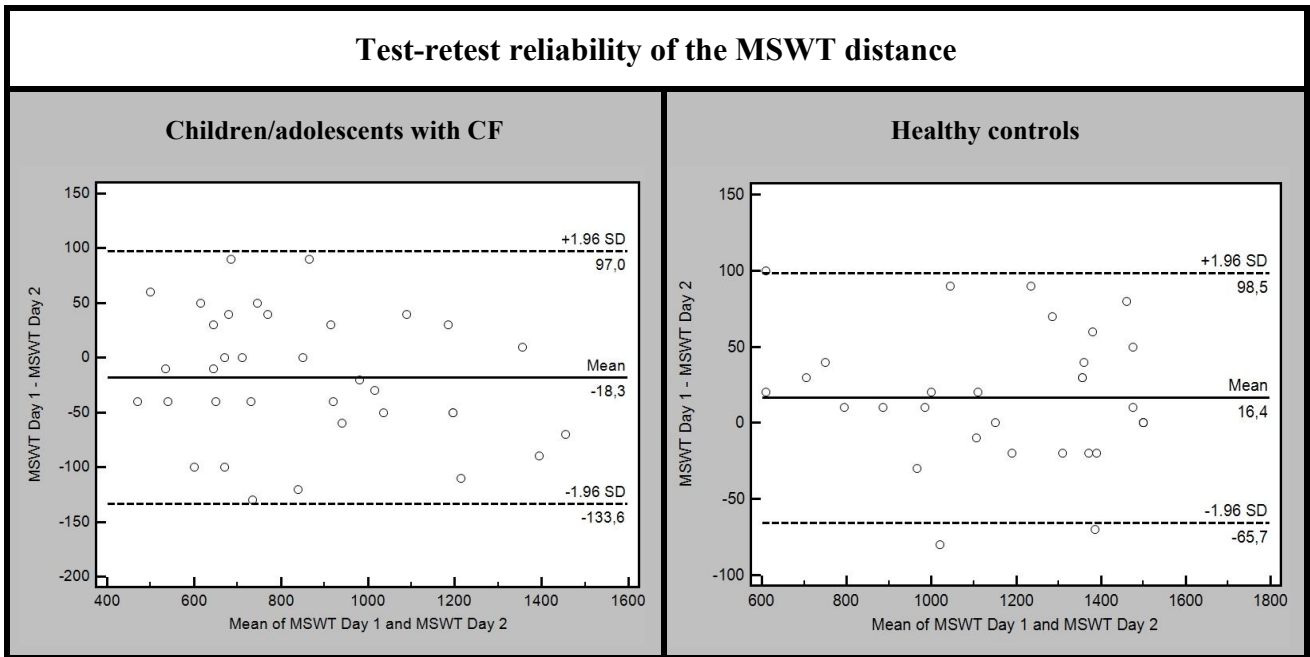
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**Table 4.** Differences in exercise tolerance and muscle strength between children/adolescents with cystic fibrosis (CF) and healthy controls.

|                        | <b>Children/adolescents with CF<br/>(n=35)</b> | <b>Healthy controls<br/>(n=34)</b> | <b>Mean difference (95%CI);<br/>Effect size (d)</b> |
|------------------------|--|------------------------------------|---|
| <b>MSWT (m)</b>        | 867.43 ± 276.2                                 | 1181.52 ± 284.16                   | -314.09 (-449.77 to -178.40);<br><i>d</i> =-1.12**  |
| <b>Dyspnoea (Borg)</b> | 4.41 ± 2.83                                    | 7.94 ± 1.03                        | -3.53 (-4.56 to -2.5);<br><i>d</i> =-1.66**         |
| <b>Fatigue (Borg)</b>  | 3.71 ± 2.13                                    | 7.85 ± 1.83                        | -4.14 (-5.1 to -3.17);<br><i>d</i> =-2.08**         |
| <b>HJT (cm)</b>        | 132.44 ± 28.9                                  | 168.36 ± 32.27                     | -35.92 (-51.92 to -19.92);<br><i>d</i> =-1.17**     |
| <b>MBT (cm)</b>        | 285.85 ± 82.56                                 | 529.58 ± 168.2                     | -243.73 (-310.98 to -176.48); <i>d</i> =-<br>1.84** |
| <b>HGL (Kg)</b>        | 14.74 ± 8.92                                   | 24.55 ± 11.76                      | -9.8 (-15.3 to -4.31);<br><i>d</i> =-0.94**         |
| <b>HGR (Kg)</b>        | 16.37 ± 8.52                                   | 25.15 ± 12.13                      | -8.78 (-14.32 to -3.24);<br><i>d</i> =-0.84**       |

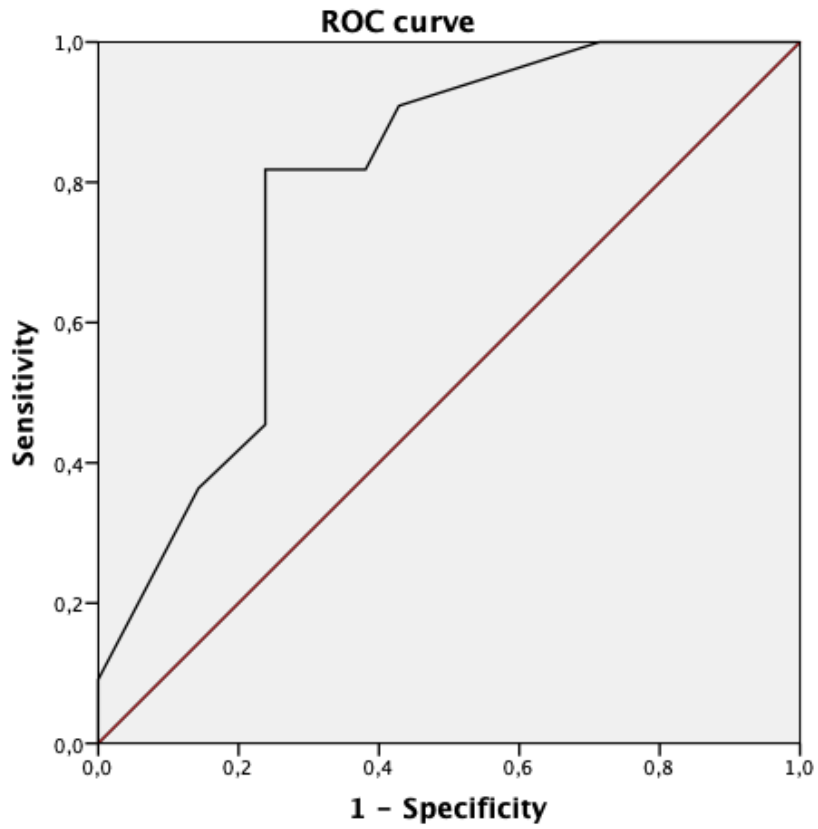
MSWT: modified shuttle walk test; HJT: horizontal jump test; MBT: medicine ball throw; HGL: handgrip strength left hand; HGR: handgrip strength right hand. \*\* *p*<.001.

**Figure 1.** Bland-Altman plots for the test-retest reliability of the MSWT distance as reported in meters. The mean difference is indicated by the solid horizontal line and the limits of agreement are demarcated by the dashed horizontal lines.



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**Figure 2.** Receiver operating characteristic (ROC) curves for the modified shuttle walk distance.



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### Highlights:

- The modified-shuttle walk test is a reliable test in children and adolescents with CF.
- The minimal detectable change for the modified-shuttle walk test is 97.08 m in children and adolescents with CF.
- There are differences in exercise tolerance and strength between children and adolescents with and without CF.