



Review

The Association of Field Test Outcomes with Peak Oxygen Uptake in Patients with Cystic Fibrosis: A Systematic Review

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ABSTRACT

International Journal of Exercise Science 15(3): 1381-1394, 2022. The purpose of the study was to evaluate the association of field test outcomes with peak oxygen uptake (VO_{2peak}) in patients with cystic fibrosis (CF) and to describe the main prediction equations available. Data searches were performed in five databases (Pubmed, Embase, LILACs, Scopus and Web of Science) and also in the reference lists of articles included. The following inclusion criteria were used: studies including individuals with CF, presenting both a field test and a cardiopulmonary exercise testing (CPET), and describing a predictive equation or coefficient of correlation/determination. Case studies, abstracts, letters of reply, editorials and duplicate publications were excluded. The methodological quality analysis was performed using the JBI Critical Appraisal Checklist for Analytical Cross-Sectional Studies scale. Protocol registration number: CRD42020148363. Ten studies were eligible. Five equations were found to predict VO_{2peak} . Equations derived from the shuttle tests (ST) showed strong correlations with VO_{2peak} ($r = 0.79$ to 0.95). The six-minute walk test (6MWT) showed moderate associations with VO_{2peak} in participants with moderate disease severity ($r = 0.53$ to 0.65). Furthermore, patients with lower maximum heart rate on the three-minute step test tended to have a higher percent predicted VO_{2peak} ($r = -0.40$), and the one-minute sit-to-stand test demonstrated moderate correlations between VO_{2peak} and the number of repetitions ($r = 0.52$ to 0.66). In conclusion, field test outcomes correlate with oxygen consumption assessed through CPET, although only the ST seems to be valid as a predictor of VO_{2peak} in patients with CF.

KEY WORDS: Exercise, cardiopulmonary exercise testing, VO_{2peak} , clinical

INTRODUCTION

Cystic fibrosis (CF) is a chronic, hereditary, progressive disease that affects multiple organs and systems (8). In the respiratory tract, the accumulation of secretions in the airways causes inflammation and frequent infections, which compromises pulmonary function and leads to the development of bronchiectasis (28, 36). Thus, exercise tolerance decreases as pulmonary

function deteriorates (24). Additionally, several peripheral muscle abnormalities have been described for patients with CF, contributing to skeletal muscle atrophy and weakness (12).

Decreased exercise capacity and functional capacity have a negative impact on CF prognosis (35). Thus, evaluating exercise tolerance is clinically relevant, given that peak oxygen uptake (VO_2peak) has strongly correlated with the occurrence of exacerbations (18) and survival (23, 38) of patients with CF. VO_2peak can be measured using the cardiopulmonary exercise test (CPET), which is considered the gold standard for assessing aerobic fitness (15, 34), as it allows for a complete and detailed evaluation of cardiovascular, respiratory, and metabolic systems, contributing to both prognosis (15) and exercise prescription (23). However, implementing the test as a clinical routine is challenging as several barriers should be overcome (33), including the requirement of expensive equipment and a highly trained team, which contributes to its underuse in several CF centers (2, 32). Therefore, field tests such as the shuttle test (ST), the six-minute walk test (6MWT), the one-minute sit-to-stand (STS) test, and the 3-minute step (STEP) test, among others, may be alternative tools for assessing exercise capacity (5, 10, 19, 37).

The use of field tests to assess aerobic fitness has grown when the gold standard (CPET) is not available, as those tests are inexpensive and easy to perform in different clinical practice settings. In addition, in some cases, the maximal effort required for CPET, especially in more severe patients, may be associated to potential adverse effects (30) and alternative submaximal tests may be required (9). However, indirect methods for VO_2peak estimation may be subject to several measurement errors, which compromises their validity (29). When field tests are used as tools to estimate oxygen uptake, the characteristics of each test, including workload and reproducibility, may significantly influence the estimation of individual oxygen uptake (20). Thus, we conducted a systematic review to evaluate the association of the main field test outcomes with oxygen uptake in patients with CF. The main field tests whose association with oxygen uptake was tested and the main prediction equations available are reported herein.

METHODS

Study design

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines (22). This review was registered with the International Prospective Register of Systematic Reviews (PROSPERO) with registration number CRD42020148363.

Search strategies

Five databases were selected according to scientific relevance: PubMed, Embase, LILACS, Scopus, and Web of Science. Additional searches were conducted on the reference lists of selected articles related to the topic. The search strategies were defined after identification of search descriptors, based on DECS (BIREME's Health Sciences Descriptors) and MESH (Medical Subject Headings, a controlled vocabulary used for indexing articles on PubMed) terms combined with the Boolean operators "AND" and/or "OR" as well as on EMBASE' controlled

vocabulary Entree descriptors. Thus, the following English-language keywords were used: Modified shuttle walk test OR incremental shuttle test OR Modified shuttle test OR Shuttle test OR Shuttle run OR Shuttle run test OR Six-minute walk test OR Six minute walk test OR 6 minute walk test OR 6-minute walk test OR three minute step test OR three-minute step test OR 3-minute step test OR 3 minute step test OR 12-minute walk test 12 minute walk test OR twelve minute walk test OR twelve-minute walk test OR 2-minute walk test OR 2 minute walk test OR two-minute walk test OR two minute walk test OR incremental step test OR One minute sit-to-stand test OR One-minute sit-to-stand test OR 1-minute sit-to-stand test OR 1 minute sit-to-stand test OR 30-seconds sit-to-stand test OR 30 seconds sit-to-stand test OR thirty-seconds sit-to-stand test OR thirty seconds sit-to-stand test OR field test AND Exercise test OR Cardiopulmonary Exercise Test OR Cardiorespiratory Fitness OR exercise tolerance OR peak oxygen uptake OR Maximal oxygen consumption AND Cystic fibrosis. No filters were used. The searches were conducted after registration with PROSPERO, from June to July 2021. The manuscript has followed the ethical standards of the International Journal of Exercise Science (21).

Article selection

Two authors (NEC and GSC) independently examined titles, abstracts, and full-text articles, when required. In cases of disagreement, a third investigator (MVFD) was invited to mediate on divergent points. After the selected descriptors were applied, duplicate studies were discarded and the following inclusion criteria were considered: (i) cross-sectional and/or longitudinal studies of individuals with CF; (ii) administration of a field test; (iii) administration of CPET as a comparator; (iv) presentation of a predictive equation or coefficient of correlation or coefficient of determination between the main field test outcome and oxygen consumption (CPET). Case reports, abstracts, letters to the editor, editorials, and duplicate publications were excluded, as well as studies that did not meet the eligibility criteria.

Data collection

All collected data were discussed between two authors (NEC and GAC). If doubt remained, a third author (MVFD) was invited to opine. The following data were collected from the selected studies and entered into an Excel spreadsheet: title, name of the first author, year of publication, country of origin, type of study, age of the participants, sample size, type of ergometer used in the laboratory test, type of protocol, oxygen uptake (VO_{2peak}), field test used, coefficient of correlation and/or determination, and equation used to predict VO_{2peak} . Whenever needed, an attempt to contact corresponding authors in order to access data was performed.

Outcomes of interest

The primary outcome of interest in this review was the correlations between oxygen uptake measured on CPET and the main outcome of each field test. The secondary outcomes was the presence of equations to predict oxygen uptake using field tests.

Quality analysis

The article quality analysis was conducted individually by two authors (NEC and FMV) using the JBI Critical Appraisal Checklist for Analytical Cross-Sectional Studies scale (25). This standardized scale consists of 8 questions and for each criterion met, the studies received 1 point (10%). Considering that questions 5 and 6 were not applicable to the studies included, 2 points (20%) were attributed to all of them. If, according to the scale, it was unclear whether the studies met a given criterion, they received 0.5 point (5%). A score from 7 to 8 (70-80%) was deemed high quality, a score 4 to 6 (40-60%) was moderate quality, and a score 0 to 3 (0-30%) was low quality. In case of disagreements or doubts, the results were discussed with a third author (MVFD) and were resolved by consensus.

Planned method of analysis

Since studies were heterogeneous and only a small number identified, meta-analysis and pooling of data were deemed inappropriate. The main variables influencing the presented equations were explored in a narrative synthesis. The validity statistic (r and/or r^2) of equations were reported, as well as the correlations between the predicted and measured VO_2peak .

RESULTS

Study selection

Of a total of 974 studies identified in the search, 235 were excluded for being duplicates and 739 remained. Of these, 714 studies were excluded for not meeting the eligibility criteria. Thus, 25 studies were eligible for full-text screening, and then 10 were included. The study selection strategy is shown in Figure 1.

Characteristics of the studies

Sample size ranged from 11 to 93 participants, and year of publication was 1996 to 2019. Regarding age groups, mean age ranged from 8 to 33 years. The included studies were all cross-sectional. The data collected from the studies are shown in Table 1.

Field tests

Shuttle tests (ST): Four studies used ST as a field test to predict VO_2peak . Three studies (3, 31, 37) administered a modified 10-m protocol (MST) and one study (31) administered two protocols (10 and 20 m) according to the age of the participants (older or younger than 7 years old). Two studies (31, 35) used a gas analyzer in the shuttle test protocols, which provided a direct measure of VO_2 . All studies demonstrated a positive correlation between the distance covered and VO_2peak measured on CPET. Correlation coefficients ranged from 0.79 to 0.95 and thus were deemed strong. One study (37) also reported a coefficient of determination for oxygen uptake estimation ($r^2 = 0.628$). Furthermore, four different equations to predict VO_2peak were extracted: (i) $\text{VO}_2 = 6.83 (2.85 \text{ to } 10.80) + 0.028 (0.019 \text{ to } 0.024) \times \text{MST distance}$; (ii) $\text{VO}_2 = [0.0289 \times \text{distance}] + 17.46$; (iii) $\text{VO}_2 = 0.8 \times \text{VO}_2 (\text{calculated}) + 8.53$; and (iv) $\text{VO}_2 = 20.301 + 0.019 \times \text{MST distance}$. These equations included distance covered (m), maximal velocity attained in the last stage of the test (km/h), "weight-age", and VO_2peak ($\text{mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$). Prediction strength was

deemed high, with correlation coefficients greater than 0.7 and without any significant differences between measured VO₂peak values and those predicted by the equations.

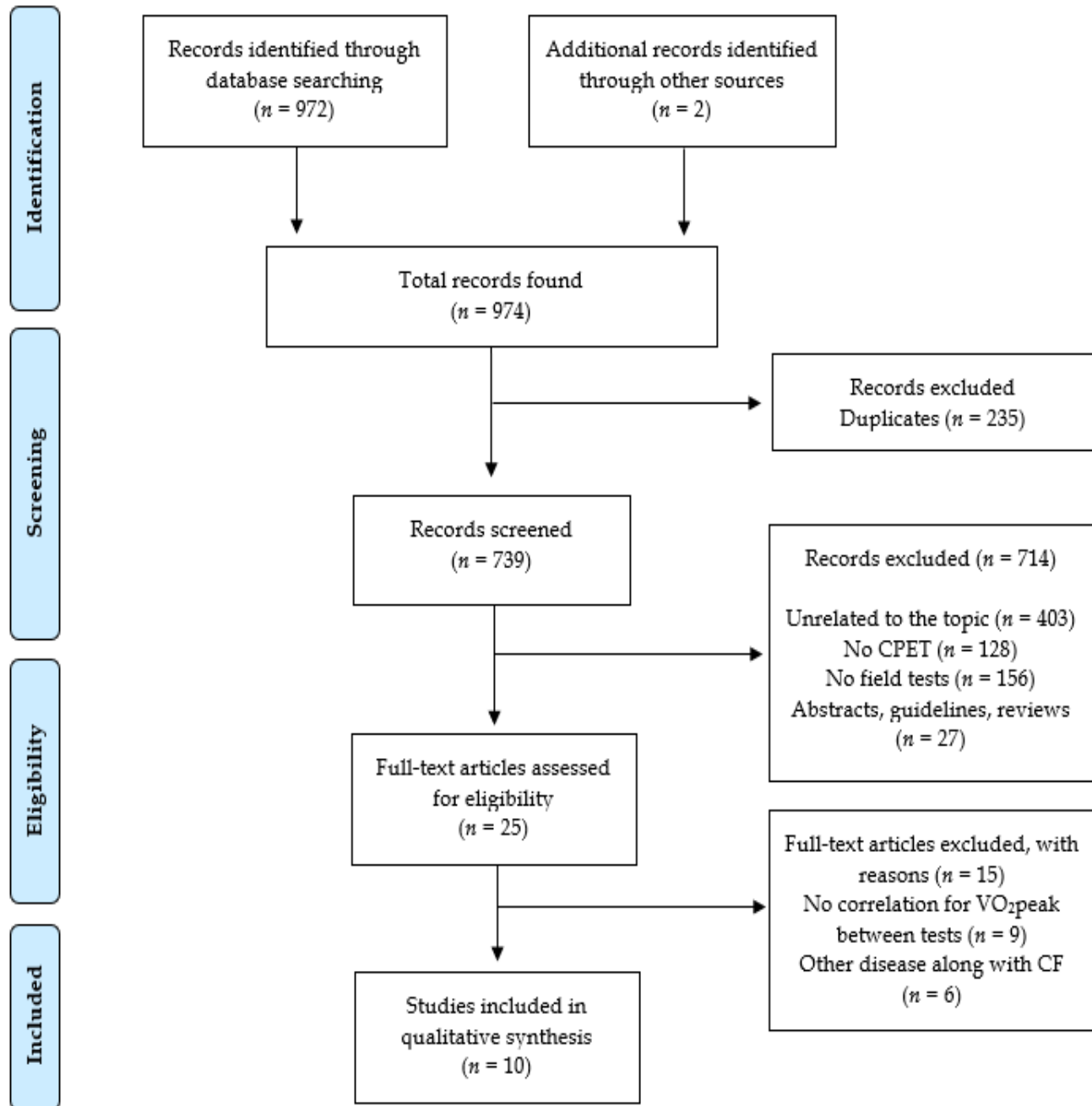


Figure 1. Flowchart of study selection.

Table 1. Main characteristics of the included studies.

	Year of publication	Country of origin	n (sex = n)	Age
Gulmans et al.1996 (13)	1996	NLD	15 (F = 6; M = 9)	14.5 ± 2.0*
Bradley et al.1999 (3)	1999	UK	20 (F = 6; M = 14)	25.0 ± 7.0*
Selvadurai et al., 2003 (31)	2003	AUS	93 (F = 35; M = 58)	11.1 (5.6-17.5)*
Lesser et al. 2010 (19)	2010	USA	11 (F = 3; M = 8)	14.3 ± 3.8*
Cohen and Orenstein 2014 (5)	2014	USA	24 (F = 9; M = 15)	12.8 (8.0-19.0)*
Gruet et al. 2016 (10)	2016	FRA	25 (F = 8; M = 17)	30.0 ± 9.0*
Radtke et al. 2016 (27)	2016	SWI	14 (F = 8; M = 6)	29.0 (25.5-36.0)#
Vallier et al. 2016 (35)	2016	FRA	20(F = 3; M = 17)	33.0 ± 8.0*
Radtke et al. 2017 (26)	2017	SWI	15 (F = 7; M = 8)	31 (25-33)#
Vendrusculo et al. 2019 (37)	2019	BRA	24 (F = 6; M = 18)	15.7 ± 4.2*

*Data presented as mean±standard deviation (or minimum-maximum values); #Data presented as median and interquartile range; n: number of patients; F: female; M: male; NLD: Netherlands; UK: United Kingdom; AUS: Austria; USA: United States of America; SWI: Switzerland; FRA: France; BRA: Brazil.

Six-minute walk test (6MWT): Three studies (10, 13, 19) used the 6MWT to assess the association between the distance walked and oxygen uptake measured on a maximal test. One of them (19) found a moderate but not significant correlation ($r = 0.65$; NS) between the distance walked on 6MWT (6MWD) and VO_2 peak. The study also found a strong and significant association between the product of body weight and distance on 6MWT (6MWORK) and VO_2 peak ($r = 0.71$; $p < .05$). Similarly, a strong and significant correlation was found between heart rate (HR) on CPET and 6MWORK ($r = 0.82$; $p < .001$). In a study (10) of adult individuals with CF, a moderate and significant correlation ($r = 0.53$; $p < .01$) was reported between the distance walked and the participants' aerobic capacity. When the distance was corrected for body weight, the correlation remained moderate ($r = 0.54$; $p < .01$). Gulmans et al., 1996 (13) demonstrated a strong correlation ($r = 0.76$; $p < .001$) of the distance walked with VO_2 peak ($mL \cdot min^{-1}$) in children with CF and moderate lung function compromise. They also found a moderate but not significant correlation ($r = 0.58$; NS) with VO_2 peak ($mL \cdot kg^{-1} \cdot min^{-1}$).

One-minute sit-to-stand (STS) test: Three studies (10, 26, 27) of adults with CF used the STS test to assess possible associations with a maximal test (27) showing a moderate correlation between VO_2 peak and STS repetitions ($r = 0.62$; $p < .001$) and recommending performing two tests for a correct assessment of functional capacity. Later, (26) demonstrated similar data in which STS repetitions presented moderate/strong correlations with VO_2 peak ($r = 0.66$; $p < .001$). According the author, the studies (27) and (26) may contain a partial overlap in the samples. Gruet et al.,

2016 (10), in turn, reported a weak correlation of the STS test with VO_2peak ($r = 0.38$; $p = .062$). However, when the repetitions were corrected for body weight, there was a moderate and significant correlation ($r = 0.52$; $p < .004$). The authors also demonstrated that the STS test had a strong correlation ($r = 0.80$; $p < .001$) with the maximal test regarding the level of oxygen desaturation.

Three-minute step (STEP) test: One study (5) compared the HR measured on both STEP and CPET, demonstrating that the STEP test had significantly lower HR values and, therefore, is a submaximal test. The study found an association of HR recovery after the STEP test with pulmonary function and CPET variables. The participants with lower maximum HR on STEP test tended to have a higher percent predicted VO_2peak ($r = -0.40$; $p = .05$). Those with a forced expiratory volume in 1 second (FEV_1) below 80% predicted took longer to return to resting HR after the STEP test ($r = 0.86$; $p < .02$). Furthermore, HR alone was sufficient to predict percent VO_2peak in children with CF, as shown in the equation $y = -0.578x + 191$.

Comparator: Regarding CPET, five studies (3, 5, 19, 31, 37) used a treadmill ergometer and five studies (10, 13, 26, 27, 35) used a cycle ergometer with incremental load protocols (Table 2). VO_2peak values ranged from 23.7 to 40.2 $\text{mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ and one study (35) only presented VO_2peak values in $\text{L} \cdot \text{min}^{-1}$. Maximum HR at the end of the test ranged from 161 to 190bpm.

Quality analysis

Regarding methodological quality, all ten studies were deemed high quality (3, 5, 10, 13, 19, 26, 27, 31, 35, 37). Two of them (3, 19) had a 0.5 point reduction for not reporting data on exclusion criteria (question 1). Also, three studies (5, 13, 31) were reduced 0.5 point for not reporting data on CPET completion (question 3). In two studies 0.5 point were reduced for not reporting information on CF diagnostic test used (26, 27). The scores ranged from 75% to 80%. Table 3 shows a detailed analysis.

Table 2. Main characteristics of cardiopulmonary exercise testing and field test protocols.

Auth ors	Cardiopulmonary exercise testing (CPET)				Field test			
	Ergometer	Protocol	VO ₂	Maximum effort criteria	Test	Protocol	r (p-value)	Equation
Gulman s et al. 1996 (13)	Cycle ergometer	ND	40.2 ± 9.1	Yes	6MWT	-	0.58 (NS)	-
Bradley et al. 1999 (3)	Treadmill	STEEP	32.8 ± 10.3	No	ST	10-m	0.95 (< .00)	VO ₂ = 6.83 (2.85 to 10.80) + 0.028 (0.019 to 0.024) XMST distance
Selvadu rai et al. 2003 (31)	Treadmill	Bruce (modified)	ND	No	MST	10-m	0.91 (ND)	VO ₂ =[0.0289xdistance] +17.46
Lesser et al. 2010 (19)	Treadmill	ND	27.0 ± 8.1	Yes	6MWT	-	0.65 (< .05)	-
Cohen and Orenstei n 2014 (5)	Treadmill	Bruce (modified)	ND	No	3-min step test	15 cm and 30 steps)	-0.40 (.05)	y= -0.578x+191
Gruet et al. 2016 (10)	Cycle ergometer	Incremental cycle	26.6 ± 6.5	Yes	6MWT	-	0.53 (< .01)	-
Radtke et al. 2016 (27)	Cycle ergometer	Godfrey	31.9 (22.6- 37.5)*	Yes	1-min STS	-	0.38 (.062)	-
Vallier et al. 2016 (35)	Cycle ergometer	ND	23.7 ± 5.8	Yes	1-min STS	-	0.62 (< .001)	-
Radtke et al. 2017 (26)	Cycle ergometer	Godfrey	1.68 (1.38- 2.29)*§	Yes	MST	10-m	0.90 (< .01)	-
Vendrus culo et al. 2019 (37)	Treadmill	Ramp (Adapted)	38.3 ± 5.9	Yes	1-min STS	-	0.66 (< .001)	-
					MST	10-m	0.79 (< .0001)	VO ₂ =20.301 + 0.019XMST distance

*Data presented as median and interquartile range; §data presented in L min⁻¹; MST: modified shuttle test; ST: shuttle test; 6MWT: six-minute walk test; VO₂: maximum oxygen consumption; r: coefficient of correlation between VO₂ measured at CPET and predicted by field tests; STEEP: standardized treadmill exponential exercise protocol; STS: seat-to-stand test; min: minute; cm: centimeter; ND: not described; NS: non-significant.

Table 3. Methodological quality of the included studies.

Studies	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Total
Gulmans et al.1996 (13)	Y	Y	U	Y	NA	NA	Y	Y	75%
Bradley et al. 1999 (3)	U	Y	Y	Y	NA	NA	Y	Y	75%
Selvadurai et al. 2003 (31)	Y	Y	U	Y	NA	NA	Y	Y	75%
Lesser et al. 2010 (19)	U	Y	Y	Y	NA	NA	Y	Y	75%
Cohen and Orenstein 2014 (5)	Y	Y	U	Y	NA	NA	Y	Y	75%
Gruet et al. 2016 (10)	Y	Y	Y	Y	NA	NA	Y	Y	80%
Radtke et al. 2016 (27)	Y	Y	Y	U	NA	NA	Y	Y	75%
Vallier et al. 2016 (35)	Y	Y	Y	Y	NA	NA	Y	Y	80%
Radtke et al. 2017 (26)	Y	Y	Y	U	NA	NA	Y	Y	75%
Vendrusculo et al. 2019 (37)	Y	Y	Y	Y	NA	NA	Y	Y	80%

NA: not applicable; U: unclear; Y: yes; Q1: Were the criteria for inclusion in the sample clearly defined?; Q2: Were the study subjects and the setting described in detail?; Q3: Was the exposure measured in a valid and reliable way?; Q4: Were objective, standard criteria used for measurement of the condition?; Q5: Were confounding factors identified?; Q6: Were strategies to deal with confounding factors stated?; Q7: Were the outcomes measured in a valid and reliable way?; Q8: Was appropriate statistical analysis used?

DISCUSSION

In this study, we sought to evaluate the association of the main field test outcomes with peak oxygen uptake in patients with CF. The results of this review show that among the evaluated tests, the ST was the only one that provided strong correlations between the distance covered and VO₂peak measured on CPET. Five different equations for predicting VO₂peak using field tests were reported.

Associations were found between all field tests and oxygen uptake measured on CPET. The studies using the ST (3, 31, 35, 37) demonstrated that in both protocols (10 and 20 m) the distance covered positively and strongly correlates with VO₂peak. Both protocols also triggered physiological responses, similar to those demonstrated on CPET, the gold standard. Vallier et al., 2016 (35) also presented HR and VO₂peak data higher in the shuttle than on CPET, and the V_E values in the shuttle without significant differences from the values found on CPET. The studies using 6MWT showed moderate correlations with VO₂peak, which may be related to the 6MWT being a submaximal test and to the study participants having moderate lung impairment (10, 13, 19). Regarding the STEP test (5), the inverse correlation found between percent VO₂peak and HR at the end of the test may be associated with submaximal characteristics, causing individuals with greater aerobic capacity to have lower HR values at the end of a submaximal test. In the studies using the STS test (10, 26, 27) positive but weak-to-moderate associations with

VO₂peak were found, which may be linked to the fact that the performance on this test depends on multiple factors such as postural control, limb muscle strength (reflecting anaerobic capacity) or local endurance, which may lessen the link with cardiorespiratory fitness.

The use of equations to predict oxygen uptake may be relevant to clinical practice, especially when CPET cannot be performed (37). This review found four equations in studies using ST, demonstrating that VO₂peak may be estimated using the test variables. In the equations generated from the 10-m ST, the regression models only included the distance covered (3, 31, 37). Only one of these studies reported the coefficient of determination, demonstrating a predictive power of 62% (37). Regarding the 20-m ST equation, VO₂peak was estimated using the velocity attained in the last stage and “weight-age” in the 50th percentile line for each patient (31). Another reported equation showed that HR at the end of STEP was able to estimate percent predicted VO₂peak. Inclusion of the participants' height caused no significant differences in the prediction values (5). Overall, the collected data show that the ST seems to be the most appropriate field test to estimate oxygen uptake in patients with CF when the CPET cannot be performed. The incremental characteristic of the ST protocol together with the test being externally paced (31) seems to have been important for those results to be achieved. However, both ST and STEP test equations were not externally validated in the respective studies. Nevertheless, it is worth noting that the use of prediction models is always associated with a margin of error, and this must be carefully considered when applying them to clinical practice.

The CPET is considered the gold standard for assessing exercise capacity in CF and should be the test of choice (14, 16). However, although field tests do not completely replace CPET, there are situations in which they can be used as alternative methods if CPET is not available. The reason is that field tests are usually inexpensive and easy to perform, and there is evidence in the literature demonstrating their important role in assessing functional capacity, exercise tolerance, and the effects of the disease on activities of daily living, among others (4, 23). One of the most used tests, the ST uses an incremental protocol that leads individuals to exhaustion, making it the most similar alternative to CPET (35). Conversely, submaximal tests seem to better reflect functional capacity and are recommended for severe cases when maximal exercise is not feasible (10). The 6MWT is the most studied submaximal test in chronic respiratory diseases (17) and the distance covered in the test has already been associated with the risk of hospitalization in children and adolescents with CF (6). Although this review showed positive correlations between the 6MWT and exercise capacity in patients with moderate disease, no equations to estimate VO₂peak have been found, which is probably related to the test being submaximal. However, two studies have shown that classifying the 6MWD by the work of walking (6MWORK) may better reflect the aerobic fitness of these patients. The STEP and the STS test are also considered submaximal (5, 29). The STEP test has already proved useful in assessing functional capacity in participants requiring lung transplantation (1). Moreover, demonstrated the possibility of predicting VO₂peak using HR post STEP, suggesting that the test could be a good option, among the submaximal tests, for assessing exercise tolerance when maximal field tests such as the ST cannot be performed. The STS test is the submaximal test that produces less hemodynamic stress for having a protocol that focuses on muscle function, as quadriceps

strength is an important variable for physical fitness performance (12, 27). The test may be able to detect oxygen desaturation but to a lesser degree and less accurately than CPET (26). In addition, the 1-min PowerSTS (STS power index) does not provide additional value on the relationship with CPET-derived maximal exercise capacity compared to STS repetitions, which should be used preferably as a measure of functional capacity and muscle function (27).

We believe it would be also important to consider the actual treatment changes in the modern era of CF, as new CFTR (cystic fibrosis transmembrane conductance regulator) modulators are increasingly impacting therapies in a daily basis, including exercise training and prescription (11). Therefore, young healthier and fitter children, as well as a new cohort of aging adults with specific comorbidities, may require changes in the rationale for exercise testing, prescription and monitoring. Early changes in exercise capacity may not be detected on field tests, especially in patients with mild-to-moderate disease. Thus, it is possible that the use of submaximal tests, as the 6MWT and the STEP test, for children and healthy young adults may no longer be useful in the near future as a tool to sufficiently stress the cardiorespiratory system and detect abnormalities. This may indicate that those tests will be gradually less associated with VO_2 peak, highlighting the use of ST, which uses an incremental protocol, externally paced and requires minimal space to be performed, consisting of an alternative tool to monitor (7) and prescribe (39) exercise whenever CPET is not available. Alternative roles as the detection of submaximal levels for exercise prescription, identification of exacerbations and evaluation of severe patients may still be contributions of field tests, with the need for individual assessment on the use of the most appropriate test for each particular clinical and severity disease presentation.

Regarding the methodological quality of the included studies, the results showed that all studies were high quality, as assessed by the JBI Critical Appraisal Checklist for Analytical Cross-Sectional Studies scale. All studies were cross-sectional and, although one study was a short communication, enough data were reported to ensure a good score.

Limitations: Our review has some limitations, including the small number of articles addressing each field test, especially the STEP test, which was reported in only one study. Additionally, sample characteristics (different age ranges and disease severity), protocols, and field tests were highly heterogeneous, which prevented us from conducting a meta-analysis.

Conclusion: Several outcome variables assessed on field tests are associated with peak oxygen uptake measured on CPET, but only the ST seems to be a valid predictor of VO_2 peak in patients with CF. Also, the severity of the disease based on pulmonary function seems to be significant for the choice of submaximal tests (6MWT, STEP test, STS test). Our findings may contribute to decision-making regarding the best method for assessing exercise capacity by health professionals responsible for managing patients with CF.

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REFERENCES

1. Aurora P, Prasad S, Balfour-Lynn I, Slade G, Whitehead B, Dinwiddie R. Exercise tolerance in children with cystic fibrosis undergoing lung transplantation assessment. *Eur Respir J* 18(2): 293–7, 2001.
2. Barker M, Hebestreit A, Gruber W, Hebestreit H. Exercise testing and training in german CF centers. *Pediatr Pulmonol* 37(4): 351-355, 2004.
3. Bradley J, Howard J, Wallace E, Elborn S. Validity of a modified shuttle test in adult cystic fibrosis. *Thorax* 54(5): 437–9, 1999.
4. Bradley J, Howard J, Wallace E, Elborn S. Reliability, repeatability, and sensitivity of the modified shuttle test in adult cystic fibrosis. *Chest* 117(6): 1666-1671, 2000.
5. Cohen S, Orenstein D. How does heart rate recovery after sub-maximal exercise correlate with maximal exercise testing in children with CF? *J Cyst Fibros* 13(6): 712-5, 2014.
6. Donadio M, Heinzmann-Filho J, Vendrusculo F, Frasson P, Marostica P. Six-minute walk test results predict risk of hospitalization for youths with cystic fibrosis: A 5-year follow-up Study. *J Pediatr* 182: 204-209, 2017.
7. Donadio MVF, Vendrusculo, FM, Campos NE, Becker NA, de Almeida IS, Queiroz, KCV, Leite, LR, Aquino, ES. The modified shuttle test as a predictor of risk for hospitalization in youths with cystic fibrosis: A two-year follow-up study. *J Cyst Fibros* 20(4): 648-654, 2021.
8. Elborn J. Cystic fibrosis. *Lancet* 388: 2519–31, 2016.
9. Gruet M, Mely L, Vallier J. Overall and differentiated sensory responses to cardiopulmonary exercise test in patients with cystic fibrosis: Kinetics and ability to predict peak oxygen uptake. *Eur J Appl Physiol* 118(9):2007-2019, 2018.
10. Gruet M, Peyré L, Mely L, Vallier, J. The 1-minute sit-to-stand test in adults with cystic fibrosis: correlations with cardiopulmonary exercise test, 6-minute walk test, and quadriceps strength. *Respir Care* 61(12): 1620–8, 2016.
11. Gruet M, Saynor Z, Urquhart D, 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* S1569-1993, 2011.
12. Gruet M, Troosters T, Verges S. Peripheral muscle abnormalities in cystic fibrosis: etiology, clinical implications and response to therapeutic interventions. *J Cyst Fibros* 16(5): 538-552, 2017.
13. Gulmans V, Van Veldhoven N, De Meer K, Helders P. The six-minute walking test in children with cystic fibrosis: Reliability and validity. *Pediatr Pulmonol* 22(2): 85–9, 1996.
14. Hebestreit H, Arets H, Aurora P, Boas S, Cerny F, Hulzebos E, Chantal K, Larry L et al. Statement on exercise testing in cystic fibrosis. *Respiration* 90(4): 332–51, 2015.
15. Herdy A, Ritt L, Stein R, de Araújo C, Milani M, Meneghelo R, Ferraz A, Hossri C et al. Cardiopulmonary exercise test: Background, applicability and interpretation. *Arq Bras Cardiol* 107: 467–81, 2016.
16. Hill K, Dolmage T, Woon L, Coutts D, Goldstein R, Brooks D. Comparing peak and submaximal cardiorespiratory responses during field walking tests with incremental cycle ergometry in COPD. *Respirology* 17(2): 278–84, 2012.

17. Holland AE, Spruit MA, Troosters T, Puhan MA, Pepin V, Saey D, McCormack MC, Carlin BW, Sciruba FC, Pitta F et al. An official European Respiratory Society/American Thoracic Society technical standard: Field walking tests in chronic respiratory disease. *Eur Respir J* 44(6): 1428-1446, 2014.
18. Kampouras A, Hatziagorou E, Kalantzis T, Avramidou V, Kontouli K, Kirvassilis F, Tsanakas, J. The fitter the better? Cardiopulmonary exercise testing can predict pulmonary exacerbations in Cystic Fibrosis. *Children* 8(6): 527, 2021.
19. Lesser D, Fleming M, Maher C, Kim S, Woo M, Keens T. Does the 6-min walk test correlate with the exercise stress test in children? *Pediatr Pulmonol* 45(2): 135-40, 2010.
20. Lang R, Stockton K, Wilson C, Russell T, Johnston L. Exercise testing for children with cystic fibrosis: a systematic review. *Pediatr Pulmonol* 55(8): 1996-2010, 2020.
21. Navalta J, Stone W, Lyons TS. Ethical issues relating to scientific discovery in exercise Science. *Int J Exerc Sci* 12(1): 1-8, 2019.
22. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, Shamseer L, Tetzlaff JM, Akl EA, Brennan SE et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews *BMJ* 372: n71, 2021.
23. Pianosi P, Leblanc J, Almudevar A. Peak oxygen uptake and mortality in children with cystic fibrosis. *Thorax* 60(1): 50-4, 2005.
24. Pianosi P, LeBlanc J, Almudevar A. Relationship between FEV1 and peak oxygen uptake in children with cystic fibrosis. *Pediatr Pulmonol* 40(4): 324-9, 2005.
25. Porrit K, Gomersall J, Lockwood C. JBI's systematic reviews: Study selection and critical appraisal. *Am J Nurs* 114(6): 47-52, 2014.
26. Radtke T, Hebestreit H, Puhan M, Kriemler S. The 1-min sit-to-stand test in cystic fibrosis – Insights into cardiorespiratory responses. *J Cyst Fibros* 16(6): 744-51, 2017.
27. Radtke T, Puhan M, Hebestreit H, Kriemler S. The 1-min sit-to-stand test-A simple functional capacity test in cystic fibrosis? *J Cyst Fibros* 15(2): 223-6, 2016.
28. Ratjen F. Cystic Fibrosis: Pathogenesis and future treatment strategies introduction pathophysiology genetics cystic fibrosis transmembrane regulator function airway surface liquid and mucociliary clearance infection and inflammation new therapies cystic fibrosis T. *Respir Care* 54(5): 595-602, 2009.
29. Rocha A, Herdy A, Souza P. Comparative analysis of direct and indirect methods for the determination of maximal oxygen uptake in sedentary young adults. *Int J Cardiovasc Sci* 32: 362-367, 2019.
30. Ruf K, Winkler B, Hebestreit A, Gruber W, Hebestreit H. Risks associated with exercise testing and sports participation in cystic fibrosis. *J Cyst Fibros* 9(5): 339-345, 2010.
31. Selvadurai H, Cooper P, Meyers N, Blimkie C, Smith L, Mellis C, Van Asperen, P. Validation of shuttle tests in children with cystic fibrosis. *Pediatr Pulmonol* 35(2): 133-8, 2003.
32. Stevens D, Oades P, Armstrong N, Williams C. A survey of exercise testing and training in UK cystic fibrosis clinics. *J Cyst Fibros* 9(5): 302-306, 2010.
33. Tomlinson O, Trott J, Williams C, Withers N, Oades P. Challenges in implementing routine cardiopulmonary exercise testing in cystic fibrosis clinical practice: A single-centre Review. *SN Compr Clin Med* 2(3): 327-331, 2020.
34. Urquhart D, Saynor Z. Exercise testing in cystic fibrosis: Who and why? *Paediatr Respir Rev* 27: 28-32, 2018.
35. Vallier J, Rouissi M, Mely L, Gruet M. Physiological responses of the modified shuttle test in adults with cystic

fibrosis. *J Cardiopulm Rehabil Prev* 36(4): 288-92, 2016.

36. Van de Weert-van P, Slieker M, Hulzebos H, Kruitwagen C, Van Der Ent C, Arets H. Chronic infection and inflammation affect exercise capacity in cystic fibrosis. *Eur Respir J* 39(4): 893-8, 2012.
37. Vendrusculo F, Heinzmann-Filho J, Campos N, Gheller M, de Almeida I, Donadio, M. Prediction of peak oxygen uptake using the modified shuttle test in children and adolescents with cystic fibrosis. *Pediatr Pulmonol* 54(4): 386-92, 2019.
38. Vendrusculo F, Heinzmann-Filho J, da Silva J, Perez M, Donadio M. Peak oxygen uptake and mortality in cystic fibrosis: Systematic review and meta-analysis. *Respir Care* 64(1): 91-8, 2019.
39. Zainuldin R, Mackey MG, Alison JA. Prescription of walking exercise intensity from the incremental shuttle walk test in people with chronic obstructive pulmonary disease. *Am J Phys Med Rehabil* 91(7): 592-600, 2012.

