A Possible Alternative Exercise Test for Youths with Cystic Fibrosis: The Steep Ramp Test

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ABSTRACT

BONGERS, B. C., M. S. WERKMAN, H. G. M. ARETS, T. TAKKEN, and H. J. HULZEBOS. A Possible Alternative Exercise Test for Youths with Cystic Fibrosis: The Steep Ramp Test. *Med. Sci. Sports Exerc.*, Vol. 47, No. 3, pp. 485–492, 2015. **Purpose**: The steep ramp test (SRT) can be used to provide an indication of exercise capacity when gas exchange measurements are not possible. This study evaluated the clinical usefulness of the SRT in adolescents with cystic fibrosis (CF) and compared the physiological responses of the SRT with the standard cardiopulmonary exercise test (CPET). **Methods**: Forty patients with CF (17 boys and 23 girls; mean ± SD age, 14.7 ± 1.7 years; forced expiratory volume in 1 s, 86% ± 18% of predicted) performed an SRT and a CPET with respiratory gas analysis in a randomized balanced design. Peak work rate (WR_{peak}), HR_{peak}, peak minute ventilation ($\dot{V}_{Epeak}$), and peak oxygen uptake ($\dot{V}O_{2peak}$) were the main outcome measures. **Results**: Patients with CF attained values for absolute and relative WR_{peak} during the SRT of 82% ± 14% and 92% ± 14% of predicted. Nutritional status and degree of airway obstruction did not influence SRT performance. Significantly higher values were attained for WR_{peak} during the SRT compared with those during the CPET (252 ± 60 vs 174 ± 46 W; $P < 0.001$), whereas significantly lower values were achieved for HR_{peak} (168 ± 14 vs 182 ± 12 bpm; $P < 0.001$), $\dot{V}_{Epeak}$ (59.2 ± 19.5 vs 72.0 ± 20.2 $L \cdot min^{-1}$; $P = 0.006$), and $\dot{V}O_{2peak}$ (36.9 ± 7.5 vs 41.5 ± 7.6 $mL \cdot kg^{-1} \cdot min^{-1}$; $P = 0.008$). A strong correlation between WR_{peak} attained at the SRT and the $\dot{V}O_{2peak}$ achieved during the CPET was found ($r = 0.822$, $P < 0.001$). **Conclusions**: The SRT seems to be a quick, convenient, and low-cost exercise test that is well-tolerated in patients with CF with mild-to-moderate airway obstruction. It provides an indication of exercise capacity and can potentially be used when exercise testing using gas exchange measurements is not possible.
Key Words: PULMONARY DISEASE, EXERCISE TESTING, EXERCISE CAPACITY, REHABILITATION, PHYSIOLOGY

Many children and adolescents with cystic fibrosis (CF) are reported to have significantly reduced exercise capacity (8,22), indicated by reduced peak oxygen uptake ($\dot{V}O_{2peak}$) values attained during a maximal cardiopulmonary exercise test (CPET). The reduced exercise capacity in patients with CF seems to have a multifactorial cause (35), in which respiratory, cardiovascular, and peripheral muscle functions are all reported as potential exercise limiting mechanisms (1). Two decades ago, Nixon et al. (29) reported significant association between exercise capacity of children and adolescents with CF and survival over 8 yr. Moreover, exercise capacity has been found to be positively linked to quality of life in CF (14). In addition, several studies have confirmed that physical activity and exercise training have many health benefits for patients with CF; it positively affects the transmembrane potential difference (20), airway mucus clearance (32), lung function on the short and long term (33), and exercise capacity (23).

Therefore, physical activity and exercise training have become increasingly important and widely accepted as cornerstones of CF management. Nowadays, performing a CPET is recommended for standard CF care and follow-up because it provides the clinician with important diagnostic, prognostic, evaluative, and functional information (30). Moreover, performing a CPET is recommended before initiation of any exercise training not only to monitor disease progression but also to detect exercise-induced limitations and therefore to provide patients with safe training recommendations (40).

Despite the clinical value of the CPET and the mentioned recommendations, premature exercise termination (e.g., due to a lack of motivation, pain, seat discomfort, and dyspnea) often limits its clinical usefulness. In addition, many CF centers currently do not perform CPET as an assessment tool for therapeutic intervention (4,37) because they do not have the equipment (metabolic cart) to directly measure $\dot{V}O_{2peak}$ (37). Because of these limitations, there is a need for less sophisticated clinical exercise testing procedures that can easily be applied in large clinics, do not put large burden on

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the cardiopulmonary system, and do not require respiratory gas analysis. This might increase the use of clinical exercise testing and exercise training in patients with CF.

Maximal and submaximal field tests not requiring respiratory gas analysis have been used to predict exercise capacity (e.g., modified shuttle test, 6-min walk test, 3-min step test). However, the 6-min walk test (25) and the 3-min step test (28) were reported to provide limited information relating to exercise capacity in children and adolescents with CF. The modified shuttle test has been found to be a reliable and valid field test in adult patients with CF (11,12). However, we identified no published studies addressing the validity and reliability of the modified shuttle test in children and adolescents with CF. Moreover, this test may have a ceiling effect when testing children and adolescents with CF with only mild-to-moderate lung dysfunction. On the other hand, the alternative 10-m shuttle walk test and the 20-m shuttle run test were reported to be reproducible and valid assessments of aerobic capacity in children and adolescents with CF (36). The steep ramp test (SRT) is another simple short-time incremental exercise test that does not require use of respiratory gas analysis measurements. The SRT is completed on a cycle ergometer up to maximal exertion, and the attained peak work rate (WR_{peak}) is its primary outcome measure. This WR_{peak} at the SRT has been reported to provide an indication of exercise capacity in different (patient) populations (6,13,27). In healthy children and adolescents, the SRT has recently been found to be a reliable and valid exercise test to predict $\dot{V}O_{2peak}$ during which the burden on the cardiopulmonary system was smaller compared with the regular CPET (6). The latter might be advantageous for patients with CF who often suffer from evident dyspnea during exercise. In addition, in children and adolescents with CF, comparable $\dot{V}O_{2peak}$ values were found during the CPET and during the SRT (38).

These findings highlight the potential for the SRT as an alternative for currently used exercise tests to provide information concerning the exercise capacity of children and adolescents with CF. Before implementing the SRT in standard medical care, knowledge concerning SRT performance in children and adolescents with CF is required. Moreover, it is important to obtain information about the characteristics of the SRT compared with the regular CPET in this patient group. Therefore, the objectives of the current investigation were 1) to evaluate the clinical usefulness of the SRT in adolescents with CF, 2) to compare the physiological response to the SRT in adolescents with CF with the response to the regular CPET, and 3) to validate the prediction equation to predict $\dot{V}O_{2peak}$ with SRT performance, as established in healthy children and adolescents, in adolescents with CF.

METHODS

Patients. Adolescents with CF between 11 and 18 yr of age and treated in the CF center of the Wilhelmina Children's Hospital, University Medical Center Utrecht, were invited to participate in the current study between January 2010 and September 2011. Body mass, body height, lung function, and exercise capacity were measured as part of routine assessments during the annual check-up. All patients were free from acute pulmonary or gastrointestinal exacerbation at the time of testing. The testing procedures used in this study met the assumptions for standard of practice for the routine care of patients with CF. Patients and their guardians provided approval for inclusion of the data acquired from these procedures in research studies. After evaluation, the medical ethical committee of the University Medical Center Utrecht determined that inclusion of the data conformed to the regulations of the Dutch CF Registration and that inclusion of the data in this study met the ethical polices of the University Medical Center Utrecht and the regulations of the Dutch government.

Anthropometric measures. Body mass (kg) and body height (m) were determined using an electronic scale (Seca 203; Seca, Hamburg, Germany) and a stadiometer (Ulmer Stadiometer; Prof. E. Heinze, Ulm, Germany) respectively. Body mass index (BMI) was calculated as the body mass divided by body height squared. SD scores were calculated for height for age, body mass for age, body mass for height, and BMI for age using Dutch normative values (34). The equation of Haycock et al. (18), validated in infants, children, and adults, was used to obtain the patient's body surface area (BSA).

Spirometry and plethysmography. Spirometry and plethysmography measurements were performed before exercise testing by qualified lung function technicians of the CF center after bronchodilation with salbutamol (800 μg). Forced vital capacity (FVC) and forced expiratory volume in 1 s (FEV_1) were obtained from flow–volume curves (Masterscreen; Jaeger, Würzburg, Germany). FEV_1 was also expressed as a percentage of FVC (Tiffeneau index). Residual volume (RV) and total lung capacity (TLC) were determined in a body plethysmograph (Master Laboratory System; Jaeger, Würzburg, Germany). The RV was expressed as a percentage of TLC (RV/TLC%) as well. The internationally used reference values of Zapletal (41) were used to express lung function values as percentage of predicted values.

Exercise testing. At least 20 min after bronchodilation with salbutamol (800 μg) for spirometry, all patients performed a CPET and an SRT on an electronically braked cycle ergometer (Lode Corival; Lode BV, Groningen, the Netherlands). Seat height was adjusted to the child's leg length, and both exercise tests were completed in a randomized and counterbalanced manner to control for a potential warming-up effect, with equal numbers of patients performing the tests as either CPET–SRT or SRT–CPET. A 15-min recovery period was completed between the two exercise tests. After the completion of both tests, the participants were asked which exercise test they preferred. During both tests, HR was determined via a 12-lead ECG (Cardioperfect; Accuramed BVBA, Herk-de-Stad, Belgium) and peripheral oxygen saturation (SpO_2) at the index finger was measured by pulse oximetry (Masimo Rad-8; Masimo Inc., Irvine, CA). Moreover,

participants breathed through a face mask (Hans Rudolph, Kansas City, MO) during the CPET and the SRT to perform breath-by-breath respiratory gas analysis and volume measurements using a respiratory gas analysis system (ZAN 600; Accuramed BVBA, Herk-de-Stad, Belgium). Gas analyzers were calibrated using gases of known concentration, whereas the flow meter was calibrated using a 3-L syringe (Hans Rudolph, Kansas City, MO). Minute ventilation ($\dot{V}E$), $\dot{V}O_2$, carbon dioxide production ($\dot{V}CO_2$), and RER were calculated from conventional equations. Output from the flow meter and gas analyzers were averaged over 10-s intervals and stored for further use. Peak exercise parameters were defined as the highest values achieved within the last 30 s before maximal exertion.

CPET. Before performing the CPET, patients rested until all measured variables were stable. During the CPET, participants started with 3 min of unloaded cycling, after which WR was increased by 10, 15, or 20 $W \cdot min^{-1}$, depending on the participant's body height (<125 cm, between 125 and 150 cm, and >150 cm, respectively) (9,15) in a ramplike manner (2, 3, or 4 W per 12 s). Patients had to maintain a pedaling frequency between 60 and 80 rpm. Peak exercise was defined as the point at which there was a sustained drop in pedaling frequency from 60 rpm despite strong verbal encouragement. A test was considered to be at or near the maximal level if at least one of the following criteria was met: HR_{peak} >180 bpm or RER at peak exercise (RER_{peak}) >1.0 (2). To measure the exhaustiveness of the CPET, the Children's OMNI Scale of Perceived Exertion was used, which has been validated in children (31). The scale starts with "0," indicating the child is "not tired at all," and ends with "10," meaning that the child is "very, very tired." The patients had to fill out the OMNI scale before and directly after the CPET to obtain a ΔOMNI score (posttest OMNI score minus pretest OMNI score). Recently constructed Dutch reference values (9) were used to express the attained WR_{peak} and $\dot{V}O_{2peak}$ during the CPET, performed according to the Godfrey (15) protocol, as a percentage of predicted.

SRT. Participants rested until all measured variables were stable. After a 3-min warm-up at 25 W, the SRT started by applying resistance to the ergometer in a ramp-like manner (2, 3, or 4 W per 2 s), resulting in increments of 10, 15, or 20 W per 10 s depending on the participant's body height (<120 cm, between 120 and 150 cm, and >150 cm, respectively) (6). The participant was instructed to maintain a pedaling frequency between 60 and 80 rpm, and peak exercise was defined as the point at which the pedaling frequency definitely dropped from 60 rpm despite strong verbal encouragement. Peak effort was confirmed when participants showed subjective signs of intense effort (e.g., unsteady biking, sweating, facial flushing, and clear unwillingness to continue despite encouragement). Before and directly after the SRT, the participants had to fill out the Children's OMNI Scale of Perceived Exertion to measure the exhaustiveness of the SRT (ΔOMNI score). The attained WR_{peak} at the SRT was compared with Dutch norm values (7) and expressed as percentage of predicted.

Statistical analysis. The Statistical Package for the Social Sciences (SPSS, version 15.0; SPSS Inc., Chicago, IL) was used analyze the data. Data are presented as mean values ± SD. Shapiro–Wilk tests were performed to confirm normal distribution of the data. As appropriate, an independent-samples *t*-test or its nonparametric equivalent, the Mann–Whitney *U* test, was performed on the anthropometric and the exercise variables to test for significant differences between boys and girls and between the SRT and the CPET. Pearson correlation coefficients were calculated between the attained WR_{peak} at the SRT and several anthropometric, lung function, and exercise variables. To validate the equation established in healthy children and adolescents to predict the $\dot{V}O_{2peak}$ attained at the CPET from SRT performance, the absolute WR_{peak} attained at the SRT by the adolescents with CF was used to predict their $\dot{V}O_{2peak}$ reached at the CPET by the following formula (6):

$$\dot{V}O_{2peak} = (8.262 \times WR_{peak}\ SRT) + 177.096$$

in which "$\dot{V}O_{2peak}$" stands for the predicted $\dot{V}O_{2peak}$ in milliliters per minute and "WR_{peak} SRT" represents the WR_{peak} attained at the SRT in W ($R^2 = 0.917$; SEE, 237.4). A Bland–Altman plot was constructed to validate this equation to predict $\dot{V}O_{2peak}$ from SRT performance in adolescents with CF. A P value <0.05 was considered statistically significant.

RESULTS

Forty-one patients were included. One 13-yr-old boy was excluded from analysis because he did not meet the subjective and objective criteria of peak performance at both exercise tests because of lack of motivation. Participant characteristics of the other 40 patients with CF are listed in Table 1 for boys ($n = 17$) and girls ($n = 23$) separately. There were no significant differences between boys and girls concerning age and anthropometric parameters. With a mean ± SD FEV_1 of 86% ± 18% of predicted and an RV/TLC% of 28% ± 10%, the total group of adolescents with CF suffered from mild-to-moderate airflow obstruction. Boys attained significantly higher absolute FEV_1 values and significantly lower RV/TLC% values compared with girls.

All 40 patients terminated the CPET and the SRT because of voluntary exhaustion, without adverse effects. They all met the subjective criteria of peak performance during the CPET and the SRT, and all but one patient attained an HR_{peak} >180 bpm and/or an RER_{peak} >1.0 during the CPET. The only patient that did not meet the latter criteria had an FEV_1 value of 45% of predicted and performed a symptom-limited CPET because of dyspnea. Table 2 presents the results of the patients with CF at the CPET and the SRT. They attained mean $\dot{V}O_{2peak}$ per kilogram values at the CPET of 93% of predicted. This indicates that, overall, the adolescents with CF had an aerobic exercise capacity within the normal range. Compared with Dutch norm values

TABLE 1. Patient characteristics.

	Boys (n = 17 (43%))		Girls (n = 23 (57%))		P Value
Clinical parameters					
Age (yr)	15.1 ± 2.1	11.2 to 18.1	14.3 ± 1.2	11.8 to 16.9	0.198
CF mutation class[a]					
Class I (n (%))	4 (24)		6 (26)		NA
Class II (n (%))	9 (53)		14 (61)		NA
Class III (n (%))	1 (6)		0 (0)		NA
Class IV (n (%))	0 (0)		1 (4)		NA
Class V (n (%))	2 (12)		0 (0)		NA
Unknown (n (%))	1 (6)		2 (9)		NA
PA colonization[b]					
Never (n (%))	6 (35)		2 (9)		NA
Free of infection (n (%))[c]	5 (29)		9 (39)		NA
Intermittent (n (%))[d]	2 (12)		5 (22)		NA
Chronic (n (%))[e]	4 (24)		7 (30)		NA
CF-related diabetes (n (%))	3 (18)		4 (17)		NA
Pancreatic insufficiency (n (%))	14 (82)		19 (83)		NA
Anthropometric parameters					
Body mass (kg)	51.5 ± 10.3	36.0 to 70.2	49.4 ± 8.8	30.0 to 63.4	0.493
Body mass for age SD score[f,g]	−0.53 ± 0.57	−1.39 to 0.51	−0.38 ± 0.99	−2.77 to 1.19	0.485
Body height (m)	1.67 ± 0.14	1.46 to 1.87	1.62 ± 0.09	1.39 to 1.78	0.211
Body height for age SD score[f,g]	−0.67 ± 0.87	−1.86 to 0.84	−0.30 ± 1.07	−2.80 to 1.69	0.345
BMI ($kg \cdot m^{-2}$)[g]	18.2 ± 1.3	16.6 to 20.2	18.6 ± 1.7	15.2 to 20.8	0.411
BMI for age SD score[f]	−0.39 ± 0.65	−1.44 to 1.10	−0.21 ± 0.74	−1.96 to 0.66	0.405
BSA (m^2)[h]	1.54 ± 0.21	1.20 to 1.90	1.48 ± 0.18	1.07 to 1.76	0.414
Lung function parameters					
FEV_1 (L)	3.15 ± 1.07	1.31 to 5.32	2.52 ± 0.69	1.33 to 3.91	0.043*
Percent of predicted[i]	91 ± 18	45 to 118	83 ± 17	51 to 112	0.169
FVC (L)[j]	3.73 ± 1.00	2.16 to 5.51	3.21 ± 0.67	1.71 to 4.42	0.083
Percent of predicted[i,j]	93 ± 13	62 to 116	90 ± 12	61 to 115	0.406
Tiffeneau index (%)[j]	80 ± 11	61 to 99	79 ± 9	64 to 93	0.761
Percent of predicted[i,j]	96 ± 13	72 to 117	94 ± 11	76 to 111	0.761
RV/TLC%[g,k]	24 ± 11	11 to 57	31 ± 8	17 to 46	0.011*

Data are presented as mean ± SD, range, or n (%).
[a]Based on the classification of CF transmembrane conductance regulator alleles used by Green et al. (16).
[b]Based on the criteria of Lee et al. (24).
[c]Free of *Pseudomonas aeruginosa* in the last 12 months.
[d]≤50% of the samples were positive for *Pseudomonas aeruginosa* in the last 12 months.
[e]>50% of the samples were positive for *Pseudomonas aeruginosa* in the last 12 months.
[f]Calculated using Dutch normative values (34).
[g]Mann–Whitney U test.
[h]Calculated using the equation from Haycock et al. (18).
[i]Calculated using reference values from Zapletal (41).
[j]FVC was not determined in one boy and two girls (n = 16 for boys and n = 21 for girls).
[k]Body plethysmography was not performed in two boys and four girls (n = 15 for boys and n = 19 for girls).
*$P < 0.05$.
NA, not applicable.

for SRT performance, adolescents with CF attained values for absolute (252 ± 60 W) and relative (5.0 ± 0.8 $W \cdot kg^{-1}$) WR_{peak} during the SRT that corresponded to 82% ± 14% and 92% ± 14% of predicted, respectively. Percentage of predicted values for WR_{peak} normalized for body mass were significantly higher than absolute WR_{peak} values, expressed as a percentage of predicted ($P < 0.001$), because of the generally decreased body weight (Table 1).

During the SRT, significantly higher values were attained for both absolute and relative WR_{peak} compared with the CPET, whereas significantly lower values at the SRT compared with the CPET were achieved for HR_{peak}, peak $\dot{V}_E$ ($\dot{V}_{Epeak}$), and $\dot{V}O_{2peak}$. The duration of the load phase of the SRT protocol was on average 2 min and 10 s, which was significantly shorter than the load phase of the CPET protocol that lasted for almost 9 min. All patients with CF indicated that they favored performing an SRT over a CPET when they were asked about their preferential maximal exercise test. This is confirmed by the objective fact that the SRT received significantly lower values for exhaustiveness (ΔOMNI) than the CPET.

To examine SRT performance in adolescents with CF in more detail, patients were divided on the basis of the degree of airway obstruction, as follows: a mild group (FEV_1, ≥80%; n = 26) and a moderate group (FEV_1, <80%; n = 14) (Fig. 1, left graph). No between-group differences were found for age (14.5 ± 1.7 vs 14.9 ± 1.7 yr, $P = 0.589$), body height (1.65 ± 0.13 vs 1.64 ± 0.08 m, $P = 0.921$), body mass (50.5 ± 10.1 vs 50.0 ± 8.2 kg, $P = 0.898$), and BMI (18.3 ± 1.5 vs 18.5 ± 1.6 $kg \cdot m^{-2}$, $P = 0.726$). Participants in the mild group had significantly lower values for the RV/TLC% (24% ± 7% vs 35% ± 11%, $P = 0.001$). There were no between-group differences in the attained absolute (83% ± 15% vs 80% ± 12% of predicted) and relative (92% ± 14% vs 91% ± 14% of predicted) WR_{peak} at the SRT (Fig. 1, left graph).

Patients with CF were also divided in subgroups on the basis of nutritional status, as follows: a group with a BMI for age SD score greater than or equal to −1.00 (n = 31) and a

TABLE 2. CPET and SRT results.

	CPET		SRT		Difference (%)	*P* Value
Time (s)[a]	536 ± 124	315 to 810	132 ± 27	75 to 195	−75	<0.001*
WR_{peak} (W)	174 ± 46	98 to 270	252 ± 60	127 to 385	+45	<0.001*
Percent of predicted	87 ± 16[b]	52 to 118	82 ± 14[c]	44 to 105	−6	0.112
WR_{peak}/kg ($W \cdot kg^{-1}$)	3.5 ± 0.6	2.4 to 4.9	5.0 ± 0.8	3.5 to 6.5	+43	<0.001*
Percent of predicted	95 ± 15[b]	70 to 127	92 ± 14[c]	67 to 117	−3	0.301
HR_{peak} (bpm)	182 ± 12	148 to 206	168 ± 14	130 to 195	−8	<0.001*
RER_{peak}[d]	1.12 ± 0.11	1.00 to 1.39	1.10 ± 0.15	0.82 to 1.42	−2	0.600
$\dot{V}E_{peak}$ ($L \cdot min^{-1}$)	72.0 ± 20.2	33 to 126	59.2 ± 19.5	17 to 126	−18	0.006**
Ventilatory reserve (%)	23 ± 20	−21 to 57	37 ± 20	−31 to 75	+61	0.005**
$\dot{V}O_{2peak}$/kg ($mL \cdot kg^{-1} \cdot min^{-1}$)	41.5 ± 7.6	23.8 to 52.3	36.9 ± 7.5	17.9 to 49.9	−11	0.008**
Percent of predicted	93 ± 15[b]	56 to 122	NA	NA	NA	
SpO_2 drop (%)[d,e]	2.1 ± 2.4	−2 to 8	1.3 ± 2.0	−1 to 7	−38	0.113
ΔOMNI[f]	6.7 ± 2.2	2.0 to 10.0	5.5 ± 2.3	0.0 to 9.0	−18	0.043***

Values are presented as mean ± SD or range.
[a]Duration of the load phase of the protocol.
[b]Calculated using reference values from Bongers et al. (9).
[c]Calculated using reference values from Bongers et al. (7).
[d]Mann–Whitney *U* test.
[e]SpO_2 determination was invalid in three boys and two girls ($n = 35$).
[f]ΔOMNI was not determined in two boys and six girls ($n = 32$).
*$P < 0.001$.
**$P < 0.01$.
***$P < 0.05$.
$\dot{V}O_{2peak}$/kg, $\dot{V}O_{2peak}$ normalized for body mass; WR_{peak}/kg, WR_{peak} normalized for body mass.

group with a BMI for age SD score less than −1.00 ($n = 9$) (Fig. 1, right graph). No differences between both groups were found for age (14.6 ± 1.7 vs 14.9 ± 1.7 yr, $P = 0.636$), body height (1.65 ± 0.11 vs 1.64 ± 0.15 m, $P = 0.873$), body mass (51.7 ± 8.7 vs 45.4 ± 10.5 kg, $P = 0.072$), FEV_1 (89% ± 16% vs 79% ± 22% of predicted, $P = 0.147$), and RV/TLC% (26% ± 8% vs 34% ± 14%, $P = 0.154$). Figure 1, right graph, shows that adolescents with CF and a BMI for age SD score greater than or equal to −1.00 attained significantly higher values for absolute WR_{peak} at the SRT (85% ± 12% vs 72% ± 16% of predicted), whereas there was no between-group difference when SRT performance was normalized for body mass (91% ± 12% vs 92% ± 19% of predicted).

Moderate-to-strong correlations were found between SRT performance (WR_{peak}) and some anthropometric variables (age, $r = 0.665$; body height, $r = 0.768$; body mass, $r = 0.746$; BSA, $r = 0.760$; with $P < 0.001$ for all coefficients), lung function variables (absolute FEV_1, $r = 0.675$; absolute FVC, $r = 0.703$; and TLC, $r = 0.669$; with $P < 0.001$ for all coefficients), and CPET variables (WR_{peak}, $r = 0.922$; $\dot{V}O_{2peak}$, $r = 0.822$; and $\dot{V}_{Epeak}$, $r = 0.763$; with P < 0.001 for all coefficients). Figure 2 depicts the strong linear relation between the absolute WR_{peak} attained at the SRT and the absolute $\dot{V}O_{2peak}$ achieved during the CPET. A strong correlation was also observed between the absolute WR_{peak} achieved at the SRT expressed as a percentage of predicted and the absolute WR_{peak} reached at the CPET expressed as a percentage of predicted ($r = 0.837$, $P < 0.001$). Between the relative WR_{peak} achieved at the SRT and the relative WR_{peak} attained at the CPET, both expressed as a percentage of predicted, a slightly lower correlation coefficient was found ($r = 0.775$, $P < 0.001$).

As depicted in Figure 3, the Bland–Altman plot demonstrates an average bias ± 1.96 SD between the predicted and the measured $\dot{V}O_{2peak}$ of −175.4 ± 309.6 $mL \cdot min^{-1}$ in our group of patients with CF. The limits of agreement were +431.4 and −782.1 $mL \cdot min^{-1}$.

DISCUSSION

The current study evaluated the clinical usefulness of the SRT in adolescents with CF and compared the physiological response to the SRT with the response to the regular CPET in this group. Moreover, the validity of the previously published prediction equation to predict $\dot{V}O_{2peak}$ with SRT

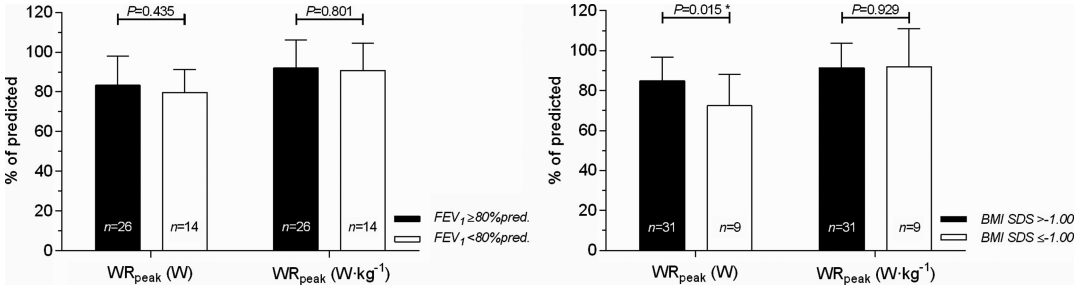

FIGURE 1—Subgroup analysis of SRT performance in children with CF. Subgroups are based on degree of airway obstruction (left graph) and nutritional status (right graph). Data are presented as mean + SD.

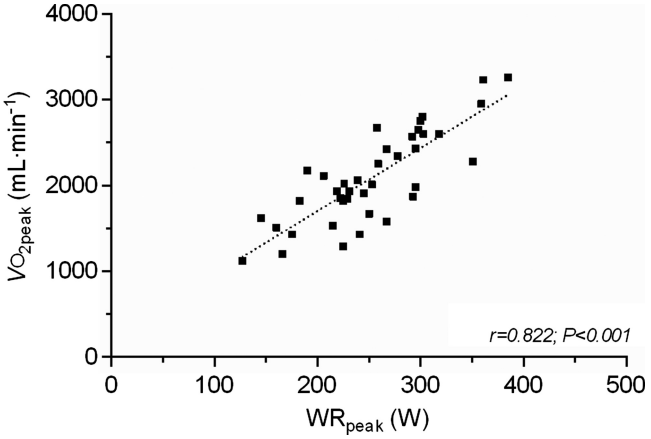

FIGURE 2—The linear relation between WR_{peak} attained at the SRT and $\dot{V}O_{2peak}$ attained at the CPET (R^2 = 0.676).

performance was investigated in adolescents with CF. We confirmed that the SRT is a feasible, short-time, incremental exercise test up to maximal exertion in adolescents with CF. They achieved values for absolute and relative WR_{peak} during the SRT corresponding to 82% and 92% of predicted. The WR_{peak} attained at the SRT correlated well with the $\dot{V}O_{2peak}$ achieved at the CPET. Perhaps, most importantly for this population, we showed that the SRT is cardiopulmonary less demanding compared with the regular CPET because significantly lower HR_{peak}, $\dot{V}_{Epeak}$, and ΔOMNI values as well as significantly higher values for the ventilatory reserve at peak exercise were found.

A *post hoc* analysis was performed to examine the effect of nutritional status and the degree of airway obstruction on SRT performance. Results show that nutritional status does not influence SRT performance when corrected for body mass, as there was no significant difference in the attained WR_{peak} at an equivalent body mass expressed as a percentage of predicted between the subgroups. Although body mass was found to be a significant predictor of absolute SRT performance, it would be interesting to examine the effect of nutritional status on SRT performance after normalizing for fat-free mass (FFM) because normalizing for body mass has been reported to overestimate the work capacity in patients with CF at the CPET. This can be explained by the greater level of fat depletion in undernourished patients with CF, resulting in higher proportion of FFM per unit of body mass (17). From a physiological perspective, FFM, as an indicator of muscle mass, would probably be a better indicator for SRT performance. We already showed this in an earlier study in healthy boys and girls, in which SRT performance was found to be best correlated to FFM (r = 0.930 and r = 0.902, respectively; $P < 0.001$ for both coefficients) (7).

The degree of airway obstruction was also found to have no influence on SRT performance. There were no significant differences in the attained absolute and relative WR_{peak} values between mildly and moderately obstructed patients with CF. However, it is possible that severe airway obstruction does limit SRT performance. Boas et al. (5) reported that the degree of airway obstruction was not a significant predictor of anaerobic exercise capacity, as measured during a Wingate anaerobic test. The authors explained this by suggesting that anaerobic exercise capacity is dependent on the anaerobic characteristics of the exercising muscles and not on oxygen transport. SRT performance also relies on anaerobic exercise capacity. In fact, with significantly higher WR_{peak} values (+45%) and significantly lower $\dot{V}O_{2peak}$ values (−11%) compared with the CPET found in the current study, it is clear that the SRT requires a substantial part of anaerobic glycolysis for energy production. This is in agreement with a recent study (38) that also reported lower $\dot{V}O_2$ values at equal WR values at the SRT compared with those at the CPET and may be explained by the slower $\dot{V}O_2$ on-kinetics observed in steeper ramp slopes, which are suggested to compromise the aerobic contribution to total energy delivery (10). Because the SRT requires a substantial part of anaerobic glycolysis for energy production as compared with the CPET, it may result in higher production of lactic acid (H^+) and, consequently, in an increase in $\dot{V}CO_2$ that augments ventilation and, therefore, the sensation of dyspnea during recovery. The latter rationale would make the SRT inappropriate for patients with severe lung dysfunction who experience evident dyspnea. However, a *post hoc* analysis of the recovery data after the SRT and CPET revealed that there were no significant differences in the recovery in the delta values of HR, RER, or $\dot{V}_E$ measured at 30 and 60 s after termination of the exercise tests (data not shown). Nevertheless, being independent of lung function combined with the lower cardiopulmonary burden at peak exercise highlights the potential of the SRT to be a clinically useful and less demanding alternative for currently used exercise tests in patients with CF.

Because of the relatively large contribution of anaerobic energy use during the SRT, this test might also serve to evaluate the effects of a high-intensity interval exercise training (HIT) program. This is also where the SRT originates from. It was introduced to determine and optimize HIT WR in adult patients with chronic heart failure (26,27). HIT might be an effective and efficient training regimen in children and adolescents with CF, especially in ventilatory-limited patients (21). Indeed, it seems that the SRT is

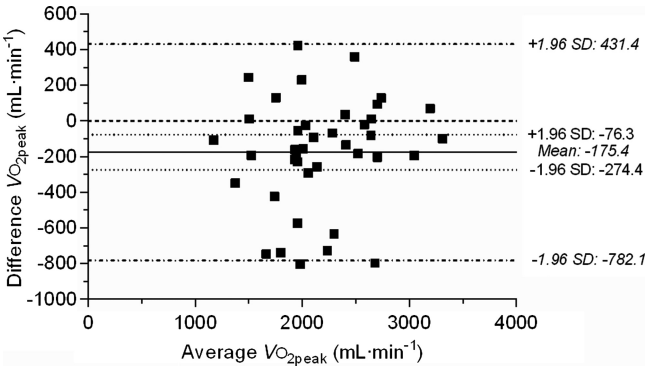

FIGURE 3—Bland–Altman plot of the $\dot{V}O_{2peak}$ at the CPET predicted from SRT performance and the measured $\dot{V}O_{2peak}$ attained at the CPET.

cardiopulmonary less demanding compared with the regular CPET because significantly lower HR_{peak}, $\dot{V}_{Epeak}$, and ΔOMNI values as well as significantly higher values for the ventilatory reserve at peak exercise were found in the current study. In addition, HIT might mimic the physical activity preferences of children and adolescents because children's physical activity patterns are characterized by short intense bursts of activity (3).

For daily clinical purposes, the SRT may be valuable as a simple screening tool that provides an indication of exercise capacity in children and adolescents with CF and mild-to-moderate pulmonary disease. Normative values for SRT performance are available for children and adolescents between 8 and 19 yr of age (7). Nevertheless, the SRT should not be used as a substitute for the more complex CPET. It is recommended to refer a child with reduced SRT performance for a regular CPET to identify possible exercise-limiting mechanisms. The equation that was established in healthy children and adolescents to predict $\dot{V}O_{2peak}$ at the CPET from SRT performance was found to overestimate the $\dot{V}O_{2peak}$ reached at the CPET in adolescents with CF. This is probably due to the fact that adolescents with CF were found to have slower $\dot{V}O_2$ kinetics (19). In addition, in contrary to what has been previously reported within our clinical exercise laboratory (38), we found a significant difference in $\dot{V}O_{2peak}$ per kilogram between CPET and SRT. This inconsistent result could be explained by the counterbalanced test sequence in the current study. Because a warming-up is thought to influence $\dot{V}O_{2peak}$ kinetics (39), warming-up effects for SRT performance are ruled out using this counterbalanced sequence. Thereby, the significant difference in $\dot{V}O_{2peak}$ per kilogram we found in this study could be explained by the more dominant oxidative metabolism of the CPET.

For future research, it would be interesting to examine SRT performance normalized for FFM in children and adolescents with CF, also in subgroups based on nutritional status, lung function, and oxygen saturation level. Therefore, it would also be interesting to examine the exact contribution of the oxidative metabolism and anaerobic glycolysis during the SRT in children with CF compared with that in their healthy peers. Further research is also needed to investigate whether the SRT could serve as a feasible alternative for evaluating exercise capacity in patients with a ventilatory limited exercise capacity who experience evident dyspnea during exercise. Finally, it would be interesting to study the responsiveness of SRT performance after HIT in children with CF to evaluate whether the SRT can be used to determine training intensity and monitor training progress.

The current study has some limitations. Although the two exercise tests were completed in a randomized and counterbalanced manner and cardiopulmonary variables returned to baseline values before the second exercise test, it is not sure whether all patients had full physiological metabolic recovery in 15 min. HR values before the start of the exercise test were not significantly different between the CPET and the SRT (103 ± 13 vs 103 ± 13 bpm; $P = 0.865$). It would therefore be relevant to investigate possible warming-up effects of both tests on each other, especially of the preceding CPET on (aerobic) SRT performance. Moreover, mainly patients with CF with mild-to-moderate airflow obstruction took part in the study. For this reason, these findings cannot be applied to patients with (other) severe lung disease. Nevertheless, the current study sample is representative for the population of patients with CF in a tertiary CF center.

CONCLUSIONS

The SRT seems to be a quick, simple, convenient, and low-cost exercise test that does not require respiratory gas analysis. Its primary outcome measure (WR_{peak}) is strongly correlated to $\dot{V}O_{2peak}$ measured during a traditional CPET in adolescents with mild-to-moderate CF. The SRT was well-tolerated by patients with CF and can potentially be used in settings where exercise testing using gas exchange measurements is not possible. However, more studies are needed to confirm our data.

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