Supramaximal Verification of Peak Oxygen Uptake in Adolescents With Cystic Fibrosis

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Purpose: To study whether peak oxygen uptake ($\dot{V}O_{2\,peak}$), attained in traditional cardiopulmonary exercise testing (CPET) in adolescents with cystic fibrosis (CF), could be verified by a supramaximal exercise test. **Methods:** Sixteen adolescents with CF (forced expiratory volume in 1 second as % of predicted [range, 45%-117%]) volunteered and successively performed CPET and a supramaximal test (Steep Ramp Test [SRT] protocol). **Results:** Cardiopulmonary exercise testing and the SRT resulted in comparable cardiorespiratory peak values. We found no significant difference in oxygen uptake ($\dot{V}O_{2\,peak}$/kg) between CPET and the SRT (38.9 ± 7.4 and 38.8 ± 8.5 mL min^{-1} kg^{-1}, respectively; $P = .81$). We found no systemic bias for CPET and SRT measurements of $\dot{V}O_{2\,peak}$/kg and no differences between CPET and SRT $\dot{V}O_{2\,peak}$ values within and between the maximal and non-maximal effort groups ($P > .4$). **Conclusion:** The $\dot{V}O_{2\,peak}$ measured in CPET seems to reflect the true $\dot{V}O_{2\,peak}$ in adolescents with CF. **(Pediatr Phys Ther 2011;23:15–21)** *Key words: adolescents, cystic fibrosis, exercise testing, exercise tolerance, pulmonary ventilation*

INTRODUCTION AND PURPOSE

Exercise testing is increasingly used to evaluate the level of exercise capacity and to define training intensity in adolescents with chronic lung diseases like cystic fibrosis (CF).[1,2] Cardiopulmonary exercise testing (CPET) is currently accepted as the gold standard to study a patient's aerobic capacity and possible limiting factors.[2,3] Most clinical exercise testing is performed with progressive workloads during cycle ergometer or treadmill exercise. During both tests, cardioventilatory parameters such as peak oxygen uptake ($\dot{V}O_{2\,peak}$), peak workload (W_{peak}), peak heart rate (HR_{peak}), and the ratio of carbon dioxide production to oxygen consumption (respiratory exchange ratio [RER]) can be calculated using gas analysis of expired air.[4]

The most important parameter of exercise capacity is the $\dot{V}O_{2\,peak}$.[2,3,5] Maximum oxygen uptake ($\dot{V}O_{2\,max}$) is considered to be the maximum attainable oxygen uptake by the cardiorespiratory and neuromuscular system, resulting in a $\dot{V}O_2$ plateau at the end of testing despite a further increase in workload.[6,7] Furthermore, $\dot{V}O_{2\,peak}$ is defined as the highest level of oxygen uptake attained during a single test without necessity of a plateau of the $\dot{V}O_2$ curve.[8] Questions can be raised about the validity of that attained $\dot{V}O_{2peak}$ during CPET in adolescents with CF, because reduced exercise capacity during CPET in adolescents with CF compared with peers without the disease has been reported.[9-12] However, the observed peak heart rates in these studies were lower than values observed in adolescents without CF. Therefore, this lower $\dot{V}O_{2\,peak}$ might be due to an actual lower $\dot{V}O_{2\,peak}$ or to an incapability of CPET to reach real $\dot{V}O_{2\,peak}$ in adolescents with CF. This

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possible inconsistency might influence the effectiveness of exercise training, while, in general, training intensity is defined on the basis of peak heart rate at the end of CPET.

Whether this attained $\dot{V}O_{2\,peak}$ reflects the true $\dot{V}O_{2\,peak}$ could be verified by a supramaximal exercise test following CPET,[7,8,13,14] where supramaximal means a workload above the peak workload attained during CPET. A feasible and safe supramaximal exercise protocol is the Steep Ramp Test (SRT), which has been developed and described as an alternative measure of exercise work rate in adult patients with chronic heart failure[15-17] and adult cancer survivors.[18] An important difference between the SRT and CPET is its short duration (about 3-4 minutes including warming-up),[18] whereas CPET will take on average 10 to 15 minutes. If consistent $\dot{V}O_{2\,peak}$ values are found in both exercise tests, this supports that a true $\dot{V}O_{2\,peak}$ has been attained.[5]

Our hypothesis is that, based on lower peak heart rates in adolescents with CF, no actual $\dot{V}O_{2\,peak}$ is reached in this population during CPET, resulting in higher $\dot{V}O_{2\,peak}$ during the SRT, which was conducted after CPET. The objective of this investigation was to verify the $\dot{V}O_{2\,peak}$ attained during CPET in adolescents with CF using an additional supramaximal exercise test (the SRT).

METHODS

Participants

Sixteen adolescents with CF (8 males and 8 females; age 14.6 ± 1.7 years) volunteered. Patients participated in a study approved by the medical ethics committee of the University Medical Center Utrecht. All patients were free from acute exacerbation at the time of testing. Patients and their parents gave written informed consent. Only the initial baseline tests before exercise training were used for analysis. Exercise testing is part of the standard follow-up in the UMC Utrecht CF center, so patients have experience with this kind of exercise testing.

Individual data were collected in 1 test session. Lung function (Master Lab System, E. Jaeger, Würzburg, Germany) and anthropometric values, using an electronic scale (Seca, Birmingham, United Kingdom) and a stadiometer (Ulmer stadiometer, Prof. E. Heinze, Ulm, Germany), were determined before CPET. Because the exercise tests were performed in the morning, participants were asked to avoid heavy meals and strenuous exercise beginning the evening before testing (12 hours before testing).

Cardiopulmonary Exercise Testing

Cardiopulmonary exercise testing was performed on an electronically braked cycle ergometer (Ergoline, Cardinal Health, Houten, the Netherlands) using the Godfrey protocol.[19] To avoid premature muscle fatigue in the adolescents, we aimed to keep total exercise time between 6 and 10 minutes. Protocols with short-stage duration, as the Godrey protocol, are preferred if the test is conducted to measure performance.[20] After 1 minute of rest, cycling started unloaded and was increased every minute independent of gender, based on height (10 W/min < 120 cm; 15 W/min 120–150 cm; 20 W/min > 150 cm), until the patient stopped volitionally because of exhaustion.[19] Adolescents breathed through a mouthpiece, connected to a calibrated metabolic cart (Oxycon pro, Care Fusion, Houten, the Netherlands). Expired gas passed through a flow meter, oxygen analyzer, and a carbon dioxide analyzer. The flow meter and gas analyzer, which were calibrated prior to each test session, were connected to a computer, which calculated breath-by-breath minute ventilation ($\dot{V}E$), oxygen consumption ($\dot{V}O_2$), carbon dioxide production ($\dot{V}CO_2$), and RER from conventional equations. Breathing reserve (BR) was calculated as $1 - [$peak minute ventilation ($\dot{V}E_{peak}$)/maximal voluntary ventilation (MVV)$]$, where MVV is calculated as $37.5 \times FEV_1$ ($L\ min^{-1}$). During testing, heart rate (HR) was monitored continuously by a 3-lead electrocardiogram (Hewlett-Packard, Amstelveen, the Netherlands), and transcutaneous oxygen saturation (SpO_2%) was measured by pulse oximetry on the index finger (Nellcor 200 E, Breda, the Netherlands). Heart rate response (HRR) was calculated as $[(HR_{peak} - HR_{rest})/(\dot{V}O_{2\,peak} - \dot{V}O_{2\,rest})]$.[21] Data were collected from 1-minute rest throughout the entire test and data were averaged and presented over 10-second time intervals. Peak exercise parameters were defined as the values achieved in the final 30 seconds before stopping.

Steep Ramp Test

The SRT was performed after a maximum of 10 minutes passive and subjective recovery following CPET and was performed on the same electronically braked cycle ergometer. A trained physical therapist (M.W.) carried out the tests and made sure that continuing testing was safe (based on recovery of SpO_2 and absence of subjective signs of excessive cardiac or ventilatory stress). A modified protocol of the SRT was used.[17] The protocol was as follows: after 1 minute of resting and 1 minute of unloaded cycling, the test started with an increase in workload every 10 seconds based on the subject's height as in CPET. The test ended when the pedal frequency fell below 60 repetitions per minute despite verbal encouragement. Exercise parameters were measured and presented using the same methodology as during CPET. *Peak exercise parameters* were defined as the values achieved during the last 10 seconds before stopping. W_{peak} was defined as the highest achieved work rate before stopping.

Definition of Maximal Effort

We used previously described criteria in our laboratory for the definition of maximum exercise effort.[8] These criteria are subdivided into subjective and objective criteria. Subjective criteria are described as "unsteady biking," "sweating," "facial flushing," and "clear unwillingness to continue despite encouragement." Objective criteria are as

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follows: (1) HR > 95% $HR_{predicted}$ (210 − age), (2) RER > 1.00, and (3) oxygen uptake plateau in the last minute. The $\dot{V}O_2$ plateau was determined from the difference between normalized $\dot{V}O_{2\,peak}$ and $\dot{V}O_2$ in the last 30 seconds of the minute before the finish. When the difference was 2.1 mL kg^{-1} min^{-1} or less, the adolescent was considered to have reached a plateau in $\dot{V}O_2$.[22] These objective criteria were created to validate that participants optimally stressed their cardiopulmonary system. A participant has to meet the subjective criteria and at least 2 of the objective criteria for the test to be considered of maximal effort and character.[8]

Statistical Analysis

Data were expressed as mean ± SD. Data were analyzed using SPSS 15.0 for Windows (SPSS Inc, Chicago, Illinois) and tested for normality with the Kolmogorov-Smirnov test. An alpha level of 0.05 was established for statistical significance. Differences between CPET and the SRT were analyzed using 1-way repeated-measures ANOVA and between the effort groups with a paired sample *t* test. Associations were examined by the Pearson product-moment correlation coefficient (*r*). Agreement between CPET and the SRT $\dot{V}O_{2\,peak}$ was verified with the Bland and Altman method.[23] Association between the difference and average $\dot{V}O_{2\,peak}$ (mL min^{-1} kg^{-1}) [(CPET $\dot{V}O_{2\,peak}$ + SRT $\dot{V}O_{2\,peak}$)!/2)] was examined by the Pearson product-moment correlation coefficient (*r*).

RESULTS

Participants

All participants (n = 16), except 1, performed both exercise tests without any complications or adverse events. The 1 participant refused to do the SRT, because of subjective feelings of fatigue. In both tests, all participants indicated that their reason to stop the exercise test was leg muscle exhaustion or fatigue. Descriptive baseline characteristics are presented in Table 1. In 3 patients, the SRT gas-exchange data were missing because of software malfunction.

TABLE 1

Study Group Demographics

Variable (n = 16)	Value (mean ± SD [range])
Age, y	14.6 ± 1.7 [12.1-17.4]
Weight, kg	50.1 ± 10.5 [30.6-67.6]
Height, cm	166.3 ± 13.6 [143.3-187.7]
Gender	8 ♀ 8 ♂
CFTR mutation	Homozygote ΔF508
Chronic Pseudomonas aeruginosa infection[a]	"yes," n = 9; "no," n = 4; "intermittent," n = 3
FEV_1 % predicted (FEV_1 (L))	81 ± 22 [45-117] (2.6 ± 1.0)

Abbreviations: CFTR, cystic fibrosis transmembrane conductance regulator; FEV_1, forced expiratory volume in 1 second.

[a]According to Leeds criteria,[34] Yes = When more than 50% of months, when samples had been taken, were *P. aeruginosa* culture positive; No = No growth of *P. aeruginosa* during the previous 12 months, having previously been *P. aeruginosa* culture positive; Intermittent = When 50% or less of months, when samples had been taken, were *P. aeruginosa* culture positive.

Comparison of Resting and Peak Exercise Variables Between CPET and SRT

All exercise variables were normally distributed. Resting HR and resting $\dot{V}E$ were significantly ($P < .01$) higher in the SRT than in CPET, whereas resting RER ($P < .01$) was significantly lower in the SRT than in CPET. No significant difference was noted for resting $\dot{V}O_2$ (mL min^{-1} kg^{-1}).

The mean exercise time of CPET was 11.0 ± 2.8 minutes and 4.1 ± 0.7 minutes for the SRT, including both 1 minute of rest measurements and 1 minute of reference cycling.

Participants reached significantly ($P < .01$) higher W_{peak} values in the SRT than in CPET, whereas RER_{peak} and HRR were significantly ($P < .01$) lower during the SRT. No other statistical significant differences in cardiorespiratory variables were found between CPET and the SRT at peak exercise (Table 2).

In addition, oxygen consumption for comparable workloads in both tests seems to be less in the SRT (Figure 1).

Correlation Between CPET and SRT Exercise Variables

Most peak exercise variables obtained during the SRT correlated excellently with those obtained during CPET ($r = 0.71–0.98$; $P < .01$). Only the decreases in SpO_2% ($r = 0.29$; $P = .33$) and $RER_{2\,peak}$ ($r = 0.06$; $P = .85$) were not significantly correlated between the SRT and CPET (Table 3).

Agreement Between the Measured Absolute and Relative $\dot{V}O_{2\,peak}$ in CPET and SRT

No systemic bias was noted for CPET and SRT measurements of $\dot{V}O_{2\,peak}$/kg values (Figure 2). The mean differences between CPET and the SRT were 0.2 L min^{-1} and 0.2 mL min^{-1} kg^{-1} for absolute $\dot{V}O_{2\,peak}$ and $\dot{V}O_{2\,peak}$/kg values, respectively. Limits of agreement between CPET and the SRT $\dot{V}O_{2\,peak}$/kg were −5.1 to 5.4 mL kg^{-1} min^{-1}.

Only fair degrees of association of CPET and SRT differences were found in $\dot{V}O_{2\,peak}$ and $\dot{V}O_{2\,peak}$/kg with CPET and SRT mean $\dot{V}O_{2\,peak}$ and $\dot{V}O_{2\,peak}$/kg ($r = -0.37$, $P = .20$; and $r = -0.42$, $P = .14$, respectively).

Maximal Effort Criteria

All participants showed all the signs of the subjective criteria. On the basis of the objective criteria, 7 participants performed a maximal effort and 8 did not. CPET HR_{peak} was missed in 1 person, so this person's performance could

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TABLE 2

Comparison of Rest and Peak Exercise Variables in CPET and the SRT[a]

Variables	CPET	SRT	Difference	%	P	η^2
Rest						
HR, beats min^{-1} (n = 12)	98.5 ± 17.9	120.6 ± 23.1	+22.1	+22.4	.00[b]	0.88
$\dot{V}O_2$, mL kg^{-1} min^{-1} (n = 13)	7.2 ± 1.8	7.5 ± 2.1	+0.3	+4.2	.53	0.03
RER, $VCO_2 \cdot \dot{V}O_2^{-1}$ (n = 13)	0.91 ± 0.06	0.85 ± 0.04	−0.06	−6.6	.00[b]	0.53
$\dot{V}E$, L min^{-1} (n = 13)	11.6 ± 4.8	13.8 ± 4.5	+2.2	19.0	.00[b]	0.54
Oxygen saturation, % (n = 13)	97.7 ± 2.2	97.3 ± 2.5	−0.4	0.4	.46	0.05
Peak exercise						
$\dot{V}O_{2\ peak}$, L min^{-1} (n = 14)	1.9 ± 0.6	1.9 ± 0.7	0	0	.81	0.01
$\dot{V}O_{2\ peak}$/kg (mL kg^{-1} min^{-1}) (n = 14)	38.9 ± 7.4	38.8 ± 8.5	−0.1	−0.3	.81	0.00
W_{peak}, Watt (n = 15)	163.0 ± 45.4	244.5 ± 71.9	81.5	+50.0	.00[b]	0.85
W_{peak}/kg, Watt·kg^{-1} (n = 15)	3.3 ± 0.5	4.9 ± 0.8	1.6	+48.5	.00[b]	0.90
HR_{peak}, beats min^{-1} (n = 13)	177.2 ± 11.9	179.2 ± 13.1	2.0	+1.1	.35	0.07
HRR (n = 12)	53.7 ± 18.6	41.5 ± 22.6	−12.2	−22.7	.00[b]	0.66
RER_{peak}, $VCO_2\ \dot{V}O_2^{-1}$, (n = 14)	1.2 ± 0.1	1.0 ± 0.1	−0.2	−16.6	.00[b]	0.59
BR, % (n = 13)	29.0 ± 14.3	30.2 ± 16.6	+1.2	+4.1	.60	0.02
$\dot{V}E_{peak}$, L min^{-1} (n = 14)	69.5 ± 25.2	70.6 ± 31.6	+1.1	+1.5	.66	0.02
Δ Oxygen saturation (n = 13)	−2.4 ± 2.5	−2.5 ± 1.5	+0.1	+4.2	.83	0.00

Abbreviatons: HR, heart rate; $\dot{V}O_2$, oxygen uptake; RER, respiratory exchange ratio; $\dot{V}E$, minute ventilation; W, work rate; HRR, heart rate response; BR, breathing reserve (%).

[a]Values are means ± SD; η^2 = partial eta squared. Δ Oxygen saturation = resting oxygen saturation − oxygen saturation at peak exercise; [b]$P < .01$.

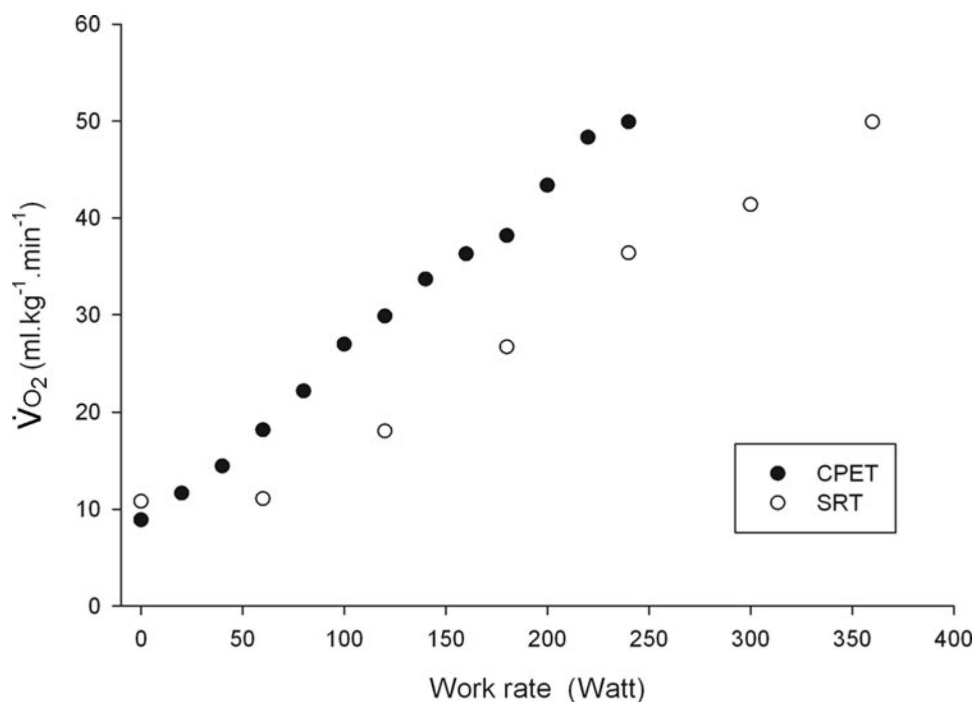

Fig. 1. Oxygen consumption as a function of work rate in CPET and the SRT. CPET, Cardiopulmonary Exercise Test; SRT, Steep Ramp Test.

not be classified according to the objective criteria. Individual data are presented in Table 4.

No differences were found between CPET and SRT $\dot{V}O_{2\,peak}$ values within the maximal and nonmaximal effort groups (P = .85 for $\dot{V}O_{2\,peak}$ and P = .54 for $\dot{V}O_{2\,peak}$/kg in the nonmaximal effort group and P = .40 for $\dot{V}O_{2\,peak}$ and P = .63 for $\dot{V}O_{2\,peak}$/kg in the maximal effort group). Furthermore, no differences were found in CPET $\dot{V}O_{2\,peak}$ values and SRT $\dot{V}O_{2\,peak}$ values between the maximal and nonmaximal effort groups (P = .62 for CPET $\dot{V}O_{2\,peak}$ and P = .46 for CPET $\dot{V}O_{2\,peak}$/kg; P = .98 for SRT $\dot{V}O_{2\,peak}$ and P = .86 for SRT $\dot{V}O_{2\,peak}$/kg). Data grouped by effort are presented in Table 5.

DISCUSSION

The objective of this investigation was to verify the $\dot{V}O_{2\,peak}$ attained during CPET in adolescents with CF using a supramaximal exercise test (the SRT). We found no significant difference in $\dot{V}O_{2\,peak}$ between CPET and

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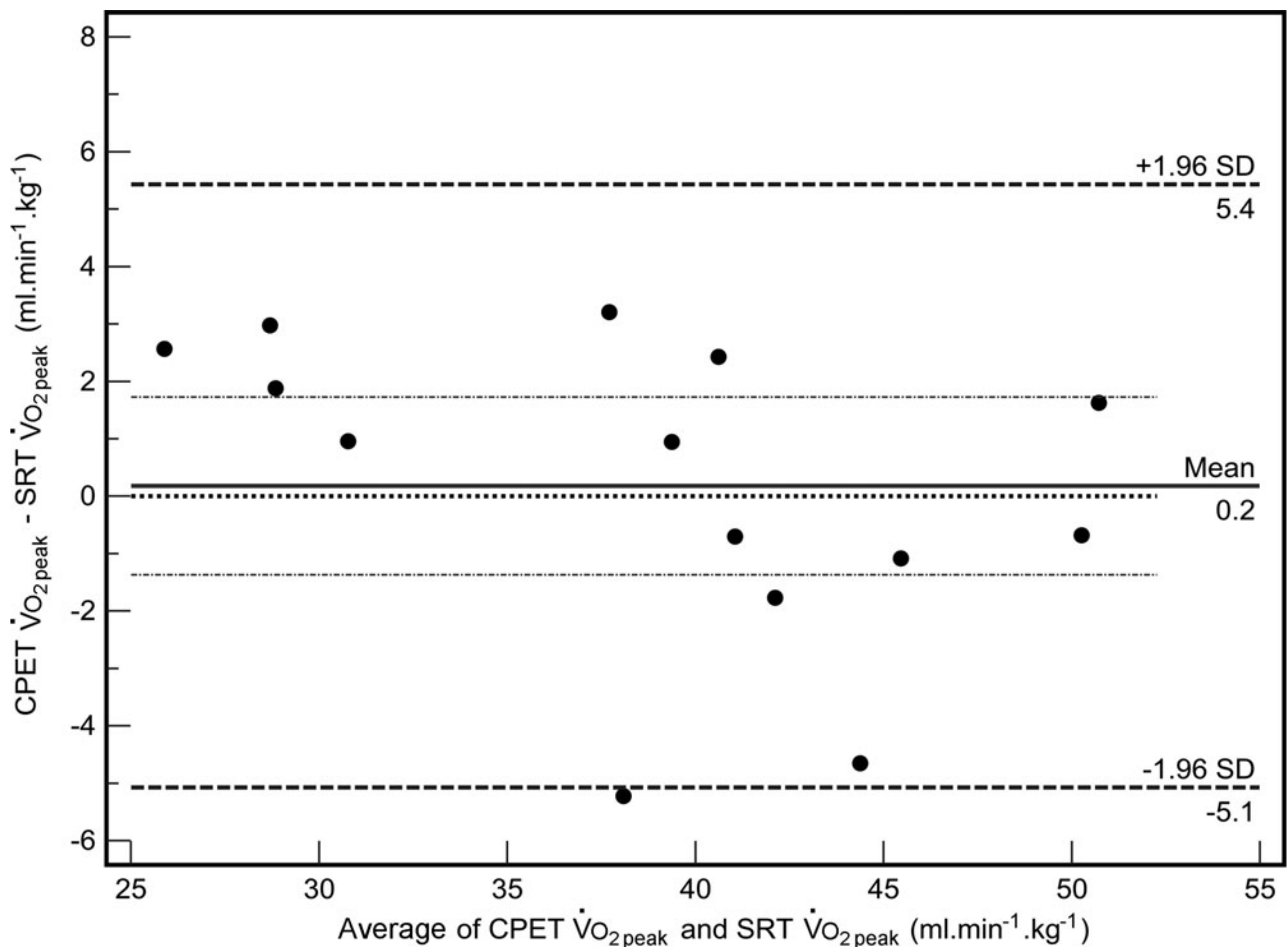

Fig. 2. Bland-Altman plot of the $\dot{V}O_{2\,peak}$ (mL min^{-1} kg^{-1}) attained during CPET and the SRT showing the bias and limits of agreement. CPET, Cardiopulmonary Exercise Test; SRT, Steep Ramp Test; $\dot{V}O_2$, oxygen uptake.

the SRT overall and when grouped on maximal effort. Our study indicates that the $\dot{V}O_{2\,peak}$ attained during CPET reflects the true $\dot{V}O_{2\,peak}$ in adolescents with mild-to-moderate CF even when the criteria for maximal effort were not met.

TABLE 3

Pearson Correlation Coefficient Between CPET and SRT Measurements

Variables	Pearson *r*
$\dot{V}O_{2\,peak}$ CPET − $\dot{V}O_{2\,peak}$ SRT (L min^{-1})	0.98[a]
$\dot{V}O_{2\,peak}$/kg CPET − $\dot{V}O_{2\,peak}$/kg SRT (mL min^{-1}kg^{-1})	0.95[a]
W_{peak} CPET − W_{peak} SRT	0.91[a]
W_{peak}/kg CPET − W_{peak}/kg SRT	0.71[a]
HR_{peak} CPET − HR_{peak} SRT	0.82[a]
RER CPET − RER SRT	0.06
$\dot{V}E_{peak}$ CPET − $\dot{V}E_{peak}$ SRT	0.97[a]
BR CPET − BR SRT	0.87[a]
Decrease in SpO_2% CPET − decrease in SpO_2% SRT	0.29

Abbreviations: $\dot{V}O_{2\,peak}$, peak oxygen uptake; W_{peak}, peak work rate; HR_{peak}, peak heart rate; RER, respiratory exchange ratio; $\dot{V}E_{peak}$, peak minute ventilation; BR, breathing reserve (%).

[a]$P < .01$; *r*, Pearson correlation coefficient.

This study extends previously reported findings in children and adolescents who are healthy,[5,7,13,14,24] and children and adolescents with spina bifida who are ambulatory.[8]

In addition, the cardiorespiratory demand of the SRT was comparable with CPET, as reflected by similar $\dot{V}E_{peak}$, HR_{peak}, and BR_{peak} values. Heart rate response was even lower in the SRT, although this can be explained by the observed higher resting HR at the start of the SRT. Although W_{peak} was significantly higher (~50%) in the SRT, and the SRT $\dot{V}O_{2\,peak}$.kg^{-1} was comparable (100.3 ± 8% of the $\dot{V}O_{2\,peak}$.kg^{-1}) to that obtained during CPET, as were other peak cardiorespiratory parameters. This indicates that our supramaximal test was more rigorous than previously used protocols using 105% to 110% of peak work rate attained during CPET,[7,14] but gave comparable results for $\dot{V}O_{2\,peak}$.kg^{-1}. Furthermore, oxygen consumption for comparable workloads seems to be less during the SRT, which can be explained by a larger portion of anaerobic metabolism in energy supply. However, to our knowledge, the validity of the SRT as a measure of exercise capacity and the validity of the SRT as a test of verification of attained $\dot{V}O_{2\,peak}$ during CPET have not been studied yet.

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TABLE 4

Individual Data on Maximal Effort Criteria

Participant	HR_{peak} (beats/min)	RER_{peak}	$\dot{V}O_{2\ peak}$/kg-$\dot{V}O_{2\ peak}$/kg Last Minute (mL min^{-1} kg^{-1})	No. of Rowland Criteria Met (of 3)	$\dot{V}O_{2\ peak}$/kg SRT − $\dot{V}O_{2\ peak}$/kg CPET (mL min^{-1} kg^{-1})
1	174[a]	1.03	−0.02	2[b]	− 1.88
2	180[a]	1.16	1.6	2[b]	− 0.68
3	183[a]	1.27	3.1[a]	1	+ 3.21
4	175[a]	1.29	3.2[a]	1	− 1.77
5	186	1.18	2.6[a]	2[b]	m.v.
6	165[a]	1.13	2.4[a]	1	− 5.22
7	196	1.22	2.1	3[b]	− 1.08
8	180[a]	1.15	2.6[a]	1	+ 1.63
9	183[a]	1.14	4.0[a]	1	+ 2.43
10	m.v.	1.21	3.4[a]	m.v.	− 4.65
11	180[a]	1.23	1.7	2[b]	+ 2.57
12	182[a]	1.14	6.4[a]	1	+ 0.95
13	155[a]	1.17	2.7[a]	1	+ 2.98
14	183[a]	1.31	0.4	2[b]	m.v.
15	192	1.12	2.7[a]	2[b]	− 0.7
16	158[a]	0.97[a]	4.3[a]	0	+ 0.96

Abbreviations: CPET, Cardiopulmonary Exercise Test; HR, heart rate; m.v., missing value; $\dot{V}O_2$, oxygen uptake; RER, respiratory exchange ratio; SRT, Steep Ramp Test.

[a]Did not meet the maximal effort criterion.

[b]Maximal effort according to criteria.

TABLE 5

Data Grouped by Effort

	No Maximal Effort	Maximal Effort
$\dot{V}O_{2\ peak}$ CPET (L min^{-1})	2.0 ± 0.7[a] (n = 8)	2.0 ± 0.6[a] (n = 7)
$\dot{V}O_{2\ peak}$ SRT (L min^{-1})	2.0 ± 0.8[a] (n = 8)	2.0 ± 0.7[a] (n = 5)
$\dot{V}O_{2\ peak}$/kg CPET (mL min^{-1} kg^{-1})	38.8 ± 6.8[a] (n = 8)	38.5 ± 9.8[a] (n = 7)
$\dot{V}E_{peak}$/kg SRT (mL min^{-1} kg^{-1})	38.2 ± 7.1[a] (n = 8)	38.1 ± 11.4[a] (n = 5)

Abbreviations: CPET, Cardiopulmonary Exercise Test; SRT, Steep Ramp Test; $\dot{V}O_2$, oxygen uptake.

[a]No differences between effort group and within effort group.

In addition, the drop in SpO_2% was comparable during CPET and the SRT, indicating that exercise-induced hypoxemia was comparable between the 2 protocols. However, we used a finger sensor that might be less sensitive comparable with a forehead sensor to detect a drop in SpO_2%.[20] On the contrary, the drop in SpO_2% should be of a very short duration during the SRT. The incremental exercise phase lasted only 2 minutes during the SRT, and the effects of oxygen desaturation should be minimal. In addition, SpO_2% was monitored during recovery and only 1 patient's SpO_2% (88%) did not recover to less than 90% within 1 minute. However, the validity of the SRT in adolescents with CF and severe arterial hypoxemia and ventricular arrhythmias is unknown and future work is needed.

Compared with known reference values obtained in Dutch adolescents who are healthy, $\dot{V}O_{2\,peak}$ and W_{peak} values during CPET were decreased (87% and 72% of predicted, respectively) in adolescents with CF.[25] This is in agreement with previous literature. Compared to adolescents with similar degrees of pulmonary dysfunction, $\dot{V}O_{2\,peak}$ and W_{peak} were higher in this study.[27-29] Comparable values were found for HR_{peak}.[29] This variously reported limited exercise capacity in adolescents with CF is suggested to have a multifactorial cause. It seems that there is an interrelationship between lung function, muscle mass, energy expenditure, (respiratory) muscle function, and exercise capacity in patients with CF.[30]

In the literature, several maximal criteria for CPET are suggested, but there is no agreement on how many criteria should be used, or the proportion that needs to be satisfied to confirm the validity of the $\dot{V}O_{2\ max}$ test results.[31] For instance, Rowland[4] suggests HR, RER, and $\dot{V}O_{2\,peak}$ plateau criteria during cycle ergometry as good indicators of maximal effort in pediatric exercise testing. The current study suggests that these guidelines from participants who are healthy might not always be valid for clinical pediatric populations. Our lower HR_{peak} data in adolescents with CF are comparable with those of other studies[9-13,32] and suggest that patients with CF have a lower HR_{peak}.

Limitations and Future Research

This study was performed in adolescents with mild to moderate CF (FEV_1 % predicted [range, 45%-117%]). The validity of the SRT as a measure of exercise capacity and the validity of the SRT as a test of verification of attained $\dot{V}O_{2\,peak}$ during CPET remain to be determined in more severe patients with CF, as well as in younger patients with CF. Furthermore, future work considering the validity of the SRT in adolescents with CF and severe arterial hypoxemia and ventricular arrhythmias is needed.

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Before the SRT, we found higher resting HR and $\dot{V}E$, accompanied by a lower RER ($P < .01$), pointing to incomplete recovery after CPET, so comparisons between resting values should be made with caution. Furthermore, a partially recovered metabolism could possibly result in a faster onset of oxygen uptake kinetics at the start of the SRT,[33] leading to a higher SRT $\dot{V}O_{2\,peak}$. Conversely, as metabolism was partially recovered and as peripheral muscle fatigue was the primary reason for ending the test, it is possible that the effect of fatigue before the SRT has influenced peak exercise parameters in this test. Nonetheless, no difference was noted in resting $\dot{V}O_2$, indicating (nearly) full metabolic recovery in the exercise parameter of interest before the SRT. To correct for the effect of test sequence, at present, we are studying the validity of the SRT to measure $\dot{V}O_{2\,peak}$ with counterbalanced test sequence.[26]

CONCLUSION

As verified with a supramaximal exercise test, the $\dot{V}O_{2\,peak}$ measured during CPET seems to reflect the true $\dot{V}O_{2\,peak}$ in adolescents with CF. The SRT seems to be an appropriate and well-tolerated protocol for the supramaximal verification of $\dot{V}O_{2\,peak}$ in adolescents with mild-to-moderate CF.

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