Substrate Utilization during and after Exercise in Mild Cystic Fibrosis

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Abstract:

Purpose: To determine substrate utilization and energy expenditure during maximal and submaximal exercise and recovery in adolescents with cystic fibrosis (CF) and healthy age-matched controls (C).

Methods: Ten clinically stable CF patients (four girls, six boys; age = 10-22 yr) were matched by body mass index, age, gender, and Tanner stage to healthy controls. Subjects completed $V \cdot O_{2peak}$ testing and submaximal exercise (20 min) on a cycle ergometer at a relative intensity of 50% $V \cdot O_{2peak}$ and at an absolute power output (PO). Metabolic parameters were assessed during exercise and recovery (20 min).

Results: Similar respiratory quotient (RQ) values occurred in both groups during maximal exercise and recovery, despite differences in the maximal PO [CF = 114 (60-180) W and C = 171 (105-280) W, P = 0.006], the total work completed [CF = 27 (9.0-54.3) kJ and C = 55 (25.3-126.5) kJ, P = 0.008], or the $V \cdot O_{2peak}$ value attained [CF = 30.6 (8.5-45.2) $mL \cdot kg^{-1} \cdot min^{-1}$ and C = 40.6 (29-64.5) $mL \cdot kg^{-1} \cdot min^{-1}$, P = 0.027]. Submaximal exercise at the same absolute PO resulted in similar RQ values during exercise and recovery despite higher heart rates and average $V \cdot O_2$ [CF = 18.8 (9.3-28.7) $mL \cdot kg^{-1} \cdot min^{-1}$ and C = 15.2 (6.5-20.1) $mL \cdot kg^{-1} \cdot min^{-1}$, P = 0.031] values in CF adolescents, and submaximal exercise at the same relative intensity also resulted in similar RQ values despite significantly greater average PO in the C group [CF = 38.7 (12.3-80) W and C = 67.8 (25.5-140) W, P = 0.039]. Excess postexercise oxygen consumption (EPOC) was greater in CF [2.79 (1.14-5.24) L O_2] than C [1.46 (0.56-2.80) L O_2] after submaximal exercise at a fixed PO (P = 0.036) but not after the relative exercise bout.

Conclusions: Habitual physical activity participation does not warrant adjustment of macronutrient intake ratios in adolescents with mild to moderate CF, but total caloric intake may need to be increased based on the level of EPOC and upon the intensity and the duration of the habitual activity.

Article:

Cystic fibrosis (CF) is an inherited, autosomal recessive, multisystem, progressive disease with an estimated median lifespan of approximately 40 yr (43). Survival for individuals with CF has consistently improved since the 1960s (13), and today patients with mild lung disease comprise an increasing percentage of individuals with CF (9). Secretions in all exocrine glands are thickened, resulting in pulmonary infection and pancreatic insufficiency (16). Blocked pancreatic ducts lead to malabsorption and malnutrition, and glucose intolerance may occur with increasing age during adolescence (16). Due to the improvements in therapy, growth retardation and wasting in patients with CF have been significantly reduced, but suboptimal nutrition is still a common clinical problem (1). Malnutrition in CF patients has been associated with lower breathing duty cycles during maximal exercise (15) and likely contributes to reduced physical activity (PA) and increased mortality (32). In patients with significant lung disease (forced expiratory volume in 1 s (FEV_1) <75%), Boucher et al. (4) found that time spent being active was significantly related to nutritional status, and other studies have shown that exercise capacity in CF may be limited by nutritional status and lung function (18,36,37,44). Several studies suggest that intrinsic changes in metabolic and functional muscle characteristics can be observed in CF patients, and these changes may or may not be linked to nutrition (25,35). As observed in healthy children, individuals with CF are most active during childhood and PA declines with age (5). Because exercise capacity may be limited in CF patients, they are particularly prone to a negative feedback loop involving compromised exercise capacity, inactivity, and deconditioning (36).

Quality of life and likelihood of survival are greater in CF patients with higher levels of aerobic fitness (23,28,31,42). Exercise has many beneficial effects for CF patients, including clearing the airway mucous (21) and stimulating the release of anabolic mediators (45). Exercise programs have been shown to improve pulmonary function and exercise capacity in individuals with CF, regardless of whether the programs are structured and supervised or unsupervised (home-based programs) (7,22,30,34,42). PA is recognized as an important therapeutic modality for CF patients, and many physicians view exercise as important for their patients and advise them to exercise (2). Optimizing nutritional status may be one mechanism to help offset the difficulties associated with regular participation in exercise and to help maintain PA levels in CF patients as they mature.

Resting energy expenditure (REE) has been reported to be elevated in CF patients by some researchers (1,33,39,41,46,47), but not others (14,19,35,48). Studies assessing energy expenditure (EE) during exercise have also produced mixed results, with some studies reporting greater exercise EE for CF patients (11,33), some reporting similar exercise EE (41,48), and one study reporting that the energy cost of activity was lower for CF patients than for controls (14). Interestingly, one study attributed the increased cost of exercise EE to increased REE (11), whereas Richards et al. (33) disagreed. However, studies directly assessing macronutrient utilization during rest, exercise, and recovery from exercise in patients with CF are very limited. Substrate utilization [from respiratory quotient (RQ) values] was found to be similar for healthy controls and patients with CF by one group (48), but another study reported greater RQ values in CF patients at rest and during exercise (41). This type of information is important because malnutrition can be problematic for these individuals and proper nutrition is important for optimal performance of habitual PA. Thus, although PA and exercise participation are helpful in managing the disease, maintaining an adequate intake of macronutrients to fuel participation is an important issue. What remains unclear is whether alterations in fat and carbohydrate (CHO) utilization occur in response to usual daily PA (submaximal exercise) in CF adolescents compared with healthy controls. Thus, the purpose of this study was to determine the substrate utilization and the energy requirements during and after maximal and submaximal constant load exercise and recovery in adolescents with CF and healthy age-matched controls. We hypothesized that adolescents with mild CF would not have significantly different substrate utilization compared with controls during any of the exercise bouts.

METHODS

Subjects and Design

Approval for all procedures was obtained from the institutional review boards of the University of North Carolina-Greensboro (UNCG) and the Wake Forest University Baptist Medical Center (WFUBMC), the Wake Forest University General Clinical Research Center (GCRC) Scientific Advisory Committee, and the WFUBMC Radiation Safety Committee. All procedures were initially tested on four healthy adolescents to ensure that instructions and directions were age appropriate. Twenty subjects [10 CF (4 girls and 6 boys) and 10 healthy matched controls (C) (4 girls and 6 boys)] aged 10-22 yr completed the study. Subjects with CF were recruited from the CF center at WFUBMC (with the assistance of Michael Schechter, MD). The study was restricted to CF patients who had mild to moderate (FEV_1% >=40%) pulmonary disease and/or exocrine pancreatic disease (treated with vitamin supplements and pancreatic enzymes). Patients were excluded if they had 1) heart problems, 2) untreated, elevated nonfasting blood glucose or CF-related diabetes, or 3) a positive pregnancy test. Patients with CF were also excluded if they had 4) FEV_1% <40% predicted, 5) needed oxygen (O_2) therapy, 6) active lung infection or treatment with intravenous antibiotics within the past month, or 7) were on the lung transplant list or had a lung transplant. A power analysis to calculate sample size for the study was chosen to detect a relative difference similar to that observed in CF adults by Ward et al. (48) and suggested a sample size of 12 subjects per group. The total number of CF patients in the CF center meeting the criteria for the study numbered 33; only 10 individuals agreed to participate in the study, a 30% recruitment rate. A cross-sectional, case-control design was used to compare the CF subjects to 10 C, matched by body mass index (BMI), age, gender, and pubertal stage and recruited from the Piedmont area.

A letter and a copy of the consent form were mailed to the family. Approximately 1 wk after the mailing, the parents and the child were called at home to answer questions, to determine interest in participating, and to schedule a time for testing. Parental informed consent and subject assent were obtained for each subject before data collection. All subjects were given a copy of the signed forms for their records. The following demographic measures were assessed: 1) pubertal stage-Tanner staging using two self-report gender-specific developmental scales for genital hair growth and penile or breast development (24); 2) daily PA using the Previous Day Physical Activity Recall (PDPAR) questionnaire (50); and 3) current health status using a brief medical history and physical screening.

Procedures

All data collection and exercise testing were completed at the GCRC at WFUBMC for the CF subjects. This facilitated enrollment and physician supervision during exercise testing. All testing of healthy adolescents was completed at the Exercise Physiology Laboratory at UNCG, except for the dual energy x-ray absorptiometry (DXA), which was completed at WFUBMC.

Data were collected during one session that lasted 7-8 h, largely because many subjects travelled considerable distances to participate in the study. Subjects ate a standardized light breakfast before arriving for testing. They completed a detailed medical history, and vital signs were measured. Nonfasting blood glucose was measured in CF subjects only using a finger prick (Life Scan Sure Step Flex; Johnson & Johnson, New Brunswick, NJ). Screening blood glucose was normal (mean = 90 $mg \cdot dL^{-1}$, range = 75-116 $mg \cdot dL^{-1}$) in all but one subject; the elevated glucose was treated and data collection was completed once blood glucose was normal. In addition, a urinary pregnancy test was completed on all female subjects who had reached menarche. Daily physical activity (PA) was measured using the PDPAR and scored accordingly (50). Briefly, subjects listed all activities, including sleep that occurred during 33 half-hour periods for the previous day and evening. Subjects also indicated how they perceived the PA in each period: 1) light, 2) moderate, 3) hard, or 4) very hard. An average daily PA score, ranging from 1 to 4, was calculated for each subject. The procedures and timing for data collection are outlined below, and the order of testing was arranged to maximize the time between the peak exercise testing and the submaximal exercise testing.

Body composition assessment.
Subjects had an accurate height (stadiometer) and weight (scale accurate to 0.1 kg) measured, and body mass index (BMI) was calculated from these measures. Dual energy x-ray absorptiometry (DXA) was completed to determine bone density and percent body fat using a Hologic Delphi A (Bedford, MA).

Resting metabolic rate.
At least 2 h after eating breakfast, subjects rested on a hospital bed in a quiet room for 30 min. Resting metabolic rate was measured for 30 min using continuous, computerized open-circuit indirect calorimetry (Sensormedics® Vmax229, Yorba Linda, CA).

Peak aerobic capacity.
A resting, supine ECG was obtained with a Quinton 710 ECG. Aerobic capacity was assessed using a Lode (Excalibur®, Netherlands) electronically braked cycle ergometer starting with a 2-min warm-up at 0 W. Initial power output (PO) was determined by height (10) and increased 10 W every minute until volitional fatigue or decreased oxygen saturation (O_{2sat}; <85%). Subjects completed a 2-min cool down at the PO of their choice and then sat quietly in a chair next to the bike for the remaining recovery measurements. Oxygen (O_2) consumption, carbon dioxide (CO_2) production, and respiratory quotient (RQ) were measured throughout the test using open-circuit spirometry (Sensormedics® Vmax229). Total energy expenditure (EE) was calculated during exercise and 20 min of recovery by summing the O_2 consumed each minute and multiplying by the standard conversion of 5 $kcal \cdot L^{-1}$ of O_2 consumed to get total caloric expenditure. Heart rate was measured throughout exercise and recovery, and RPE was recorded at the end of each minute of exercise. Total work was calculated as the sum of the Watts completed per minute during the maximal exercise test and converting this value to kilojoules using standard conversions (20). PO for the submaximal exercise sessions was determined by calculating 50% of the $V \cdot O_{2peak}$ value. Once this value was obtained, the PO that produced this $V \cdot O_2$ value was

determined, and this PO was used in the relative submaximal exercise session. Respiratory equivalents (V·E/V·O_2 and V·E/V·CO_2) were calculated and graphed for the first five stages of maximal exercise only because stages beyond this point had only a few subjects.

Relative submaximal exercise session.

Approximately 2 h after eating a standardized snack and 2-3 h after the peak exercise test, a constant load submaximal exercise test was done using a Lode Excalibur® electronically braked cycle ergometer. The test began with a 2-min warm-up at 0 W, with an increase in PO that was calculated to produce 50% V·O_{2peak} from the peak aerobic exercise test. Subjects exercised for 20 min or until a decrease in oxygen saturation (O_{2sat}; $<85\%$) occurred. When necessary, PO was decreased so that subjects could exercise for 20 min. Reductions in PO were necessary in three CF subjects and three C subjects, with an average reduction of 10-15 W for both groups. One subject had difficulty maintaining an even pedaling cadence, which resulted in widely varying V·E and V·O_2 values from minute to minute, and the data for this subject were eliminated from the analyses related to these measures. Heart rate was measured throughout the exercise and recovery, and RPE was noted at 1, 5, 10, 15, and 20 min of exercise. Exercise and recovery O_2 consumption, CO_2 production, ventilation, and RQ were measured using open-circuit spirometry (Sensormedics® Vmax229). Upon completion of the 20-min exercise session, subjects were immediately moved to a chair and were asked to rest quietly for the recovery measurements. The percentages of fat and CHO utilization were calculated using standard nonprotein RQ conversion tables for the exercise and the recovery data (20). The average PO was calculated as total work divided by 20 min. Calculations of excess postexercise oxygen consumption (EPOC) were made as described by Short and Sedlock (40), with consideration for resting O_2 consumption. Respiratory equivalents (V·E/V·O_2 and V·E/V·CO_2) were calculated and graphed for minutes 1, 5, 15, and 20.

Absolute submaximal exercise session.

On a separate occasion, 7 of the 10 healthy, age-matched control subjects returned to the Exercise Physiology Laboratory at UNCG to complete a second submaximal exercise test. At least 2 h after eating a standardized snack, subjects completed a 2-min warm-up at 0 W, and then PO was increased to the same level as that of the CF patient who was matched to the control. This second submaximal exercise session allowed us to address differences in substrate utilization between the two groups at the same absolute workload.

Pulmonary function tests (PFT).

Severity of pulmonary disease was measured by PFT, obtained according to American Thoracic Society guidelines by trained spirometry technicians every 3 months for all patients in the CF center as part of routine medical care. The Knudsen Regression Equation in the computerized database accounted for gender, racial, height, and weight differences in calculating PFT. Pulmonary function chart data from the last clinic visit (within the past 3 months) were used to classify severity of pulmonary disease. The specific PFT used were 1) percent predicted FEV in the first second (FEV_1% predicted), 2) forced vital capacity (FVC% predicted), 3) FEV_1-FVC ratio, and 4) FEF_{25-75} ($FEF_{25-75\%}$ predicted), forced expiratory flow from 25% to 75% of FVC% predicted. PFT and MVV were assessed on the day of testing with the Sensormedics® Vmax229 gas analyzer in all subjects. Oxygen saturation (O_{2sat}) was obtained using a pulse oximeter; CF subjects were monitored continuously for O_{2sat} throughout the exercise testing.

Statistics

Descriptive statistics and exercise data presented include the mean (range). CF and matched normal controls were compared using the Wilcoxon signed rank test as the differences were usually not normally distributed. Statistical significance was set at $P < 0.05$, but no adjustment for multiple comparisons was made. The P values are reported as a form of descriptive statistics.

RESULTS

Subject characteristics are shown in Table 1. Groups were matched on age and Tanner stage, but adolescents with CF were significantly smaller (height and weight) than the healthy adolescents despite similar BMI values. Although smaller height and weight could indicate potential growth delays or inadequate nutrient absorption in the CF group, this was not reflected by percent body fat values, which were similar for both groups [18.2% (10.6-25.1%) vs 20.7% (12.9-31.1%) for CF and C, respectively, P = 0.33]. No difference in pubertal development was present as measured by the self-report Tanner scale, and REE was similar for both groups. Both groups reported moderate daily PA from the PDPAR assessment [2.03 (1.39-3.95) and 2.06 (1.57-3.18) for CF and C, respectively, P = 0.49].

	CF (N = 10)	C (N = 10)	P Value
Age (yr)	14.5 (10–22)	13.8 (10–19)	0.25
Ht (cm)	155.5 (127.9–7.3)	161.7 (143.5–178.8)	0.002
Wt (kg)	44.4 (24.6–59)	50.5 (33.4–64.4)	0.010
BMI ($kg \cdot m^{-2}$)	18.0 (14.8–22.2)	19.0 (15.8–21.5)	0.11
% body fat—DXA	18.2 (10.6–25.1)	20.7 (12.9–31.1)	0.33
Resting heart rate (bpm)	81.3 (60–109)	70.8 (48–92)	0.14
Resting systolic BP (mm Hg)	110.7 (95–127)	108.0 (96–128)	0.16
Resting diastolic BP (mm Hg)	66.5 (54–86)	61.0 (46–72)	0.79
FEV_1 predicted (%)	77.5 (45–123)	91.0 (70–110)	0.19
FVC predicted (%)	89.4 (63–125)	101.0 (73–125)	0.12
FEF_{25-75} predicted (%)	61.3 (19–116)	83.0 (39–110)	0.19
Respiratory rate ($breaths \cdot min^{-1}$)	20 (12–32)	18 (14–21)	0.53
Tanner score scale 1	3.5 (1–5)	3.4 (1–5)	1.0
Tanner score scale 2	3.6 (1–5)	3.3 (1–5)	0.53
PA score (PDPAR)	2.03 (1.39–3.95)	2.06 (1.57–3.18)	0.49
Resting EE ($kcal \cdot d^{-1}$)	1539 (1161–2209)	1532 (1080–2200)	0.63

Values are presented as mean (range).

Comparisons of the PFT are also presented in Table 1. Mean FEV_1% predicted for the CF group was 77.5%, indicating mild CF [four had FEV_1% >40-69%, four had FEV_1% 70% to <90%, and two had normal lung function]. Control subjects had no known lung disease, but four had reduced FEV_1% (70-87%), likely due to inexperience with performing PFT. The 13.5% mean difference in FEV_1% between groups was not significant, but the range within the CF group was nearly twice that of the C group. Breathing reserve index at maximal exercise (BRI_{max}; $V{\cdot}E_{max}$/MVV) was similar for the two groups [0.70 (0.46-1.01) compared with 0.69 (0.41-0.92) for CF and C, respectively, P = 0.98].

The results from the peak aerobic capacity testing are presented in Table 2. As expected, CF patients were significantly more unfit than the C group, with lower maximal PO, total work, total exercise energy expenditure (EE), and $V{\cdot}O_{2peak}$ values expressed in either milliliters per kilogram per minute [30.6 (8.5-45.2) vs 40.6 (29-64.5) $mL{\cdot}kg^{-1}{\cdot}min^{-1}$, P = 0.027] or liters per minute [1.33 (0.43-2.37) vs 2.09 (1.15-3.96) $L{\cdot}min^{-1}$, P = 0.004]. Maximal and recovery RQ values were similar in the two groups. Blood pressure and RPE responses were also similar for the groups, but heart rate and time to reach resting $V{\cdot}O_2$ during recovery were significantly greater in the C group.

	CF (*N* = 10)	C (*N* = 10)	*P* Value
Maximum heart rate (bpm)	177.5 (138–200)	195.8 (183–205)	0.004
Maximum systolic BP (mm Hg)	133.8 (108–170)	143.0 (110–116)	0.37
Maximum diastolic BP (mm Hg)	73.8 (62–84)	70.2 (50–82)	0.72
Maximum RPE	18 (13–20)	18 (14–20)	0.69
Maximal PO (W)	113.5 (60–180)	170.5 (105–280)	0.006
$\dot{V}O_{2peak}$ ($L{\cdot}min^{-1}$)	1.33 (0.43–2.37)	2.09 (1.15–3.96)	0.004
$\dot{V}O_{2peak}$ ($mL{\cdot}kg^{-1}{\cdot}min^{-1}$)	30.6 (8.5–45.2)	40.6 (29–64.5)	0.027
Total exercise EE (kcal)	31.3 (8.2–73.3)	78.5 (23.8–266.2)	0.004
BRI ($\dot{V}_E$/MVV)	0.70 (0.46–1.01)	0.69 (0.41–0.92)	0.98
RQ_{max}	1.1 (0.98–1.29)	1.1 (1.03–1.17)	0.44
5-min recovery RQ (average 1–5 min)	1.22 (1.04–1.35)	1.21 (1.10–1.3)	0.57
20-min recovery RQ (average 6–20 min)	0.89 (0.76–0.98)	0.89 (0.78–0.95)	0.70
Total work (kJ)	27 (9.0–54.3)	55 (25.3–126.5)	0.008
Time to resting $\dot{V}O_2$ (min)	7.7 (4–20)	10.9 (7–20)	0.008

Values are presented as mean (range).

Figure 1 demonstrates the O_2 consumption patterns for the CF group and for the C group during the relative and the absolute submaximal exercise testing sessions and for the 20 min of recovery from submaximal exercise. The pattern of O_2 consumption was similar for all exercise sessions, and although O_2 consumption was greater during recovery in the CF subjects, the pattern was similar to that observed for the C group. Calculations of total O_2 consumed during recovery (L O_2) revealed that both groups had similar EPOC after the relative submaximal exercise session

[2.7 (1.95-5.24) and 2.1 (1.39-3.24) L O_2; $P = 0.16$] (Table 3), but that EPOC was significantly greater in the CF group after the absolute submaximal exercise session [2.79 (1.14-5.24) vs 1.46 (0.56-2.80) L O_2, $P = 0.036$] (Table 4).

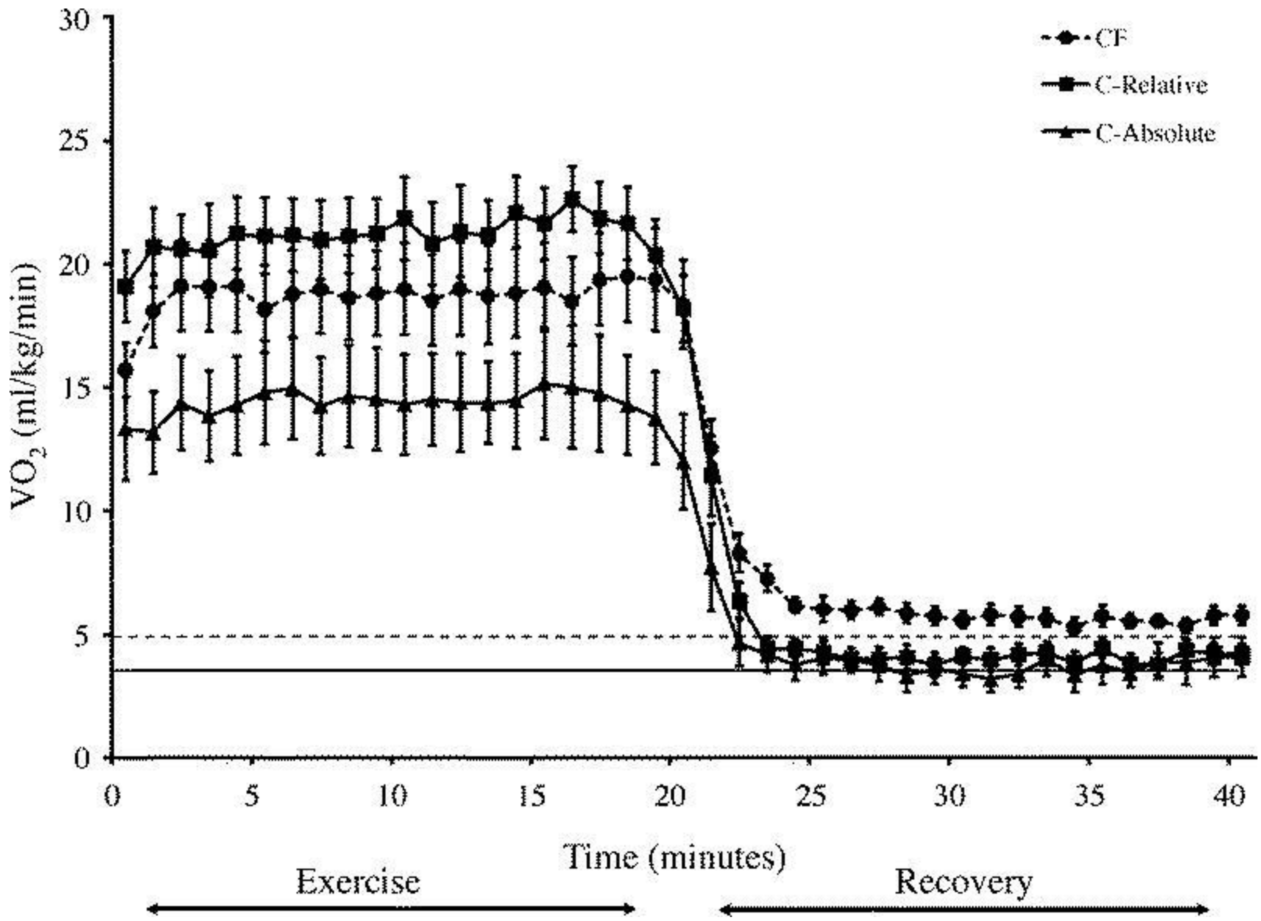

FIGURE 1-Profiles of O_2 consumption ($V{\cdot}O_2$) during 20 min of submaximal exercise and 20 min of recovery in patients with CF (solid circles) and at the same relative intensity (50% $V{\cdot}O_{2peak}$) in controls (solid squares) and with controls working at the same absolute PO (solid triangles). Mean resting $V{\cdot}O_2$ values are shown for CF (dotted line) and controls (solid line). Values are presented as mean ± SD.

	CF (N = 10)	C (N = 10)	P Value
Maximal heart rate (bpm)	149 (123–178)	159 (142–188)	0.19
Maximum systolic BP (mm Hg)	125.6 (110–154)	131.6 (110–150)	0.39
Maximum diastolic BP (mm Hg)	68.6 (58–80)	68.2 (58–84)	0.92
Maximum RPE	14.2 (7–19)	14.0 (10–18)	0.84
Average PO ($W \cdot min^{-1}$)	38.7 (12.3–80)	67.8 (25.5–140)	0.039
Average $\dot{V}O_2$ ($L \cdot min^{-1}$)	0.82 (0.48–1.49)	1.08 (0.62–1.90)	0.13
Average $\dot{V}O_2$ ($mL \cdot kg^{-1} \cdot min^{-1}$)	18.8 (9.3–28.7)	21.1 (14.6–31.1)	0.49
% $\dot{V}O_{2peak}$	60.3 (50.1–69.4)	53.2 (40.0–67.5)	0.12
Total exercise EE (kcal)	69.7 (28.7–144.1)	107.8 (61.0–190.5)	0.037
Total work (kJ)	46.6 (14.8–96.4)	81.7 (30.7–167.7)	0.039
Average RQ	0.93 (0.87–1.00)	0.94 (0.91–0.98)	0.77
5-min recovery RQ (average 1–5 min)	0.92 (0.84–0.97)	0.95 (0.92–1.01)	0.13
20-min recovery RQ (average 6–20 min)	0.88 (0.82–0.98)	0.90 (0.80–1.0)	0.32
EPOC magnitude (L O_2)	2.7 (1.95–5.24)	2.1 (1.39–3.24)	0.16
Time to resting $\dot{V}O_2$ (min)	7.5 (1.0–20.0)	8.8 (4.0–20.0)	0.63

Values are presented as mean (range).

TABLE 3. Submaximal exercise and recovery results for the adolescents with cystic fibrosis (CF) and healthy, matched controls (C) when relative intensity was set at 50% of $V \cdot O_{2peak}$.

	CF (N = 7)	C (N = 7)	P Value
Maximal heart rate (bpm)	152.4 (130–178)	136.9 (105–151)	0.047
Maximum systolic BP (mm Hg)	127.3 (110–154)	125.4 (114–132)	0.66
Maximum diastolic BP (mm Hg)	68.7 (60–80)	72.6 (60–80)	0.44
Maximum RPE	13.6 (7–17)	11.6 (8–16)	0.69
Average PO ($W \cdot min^{-1}$)	34.2 (12.3–80)	38.3 (12.2–80)	0.88
Average $\dot{V}O_2$ ($L \cdot min^{-1}$)	0.77 (0.48–1.49)	0.76 (0.31–1.30)	0.81
Average $\dot{V}O_2$ ($mL \cdot kg^{-1} \cdot min^{-1}$)	18.8 (9.3–28.7)	15.2 (6.5–20.1)	0.016
% $\dot{V}O_{2peak}$	59.6 (50.1–69.4)	46.6 (28.9–68.3)	0.012
Total exercise EE (kcal)	73.9 (42.9–144.1)	72.5 (23.3–127.9)	1.0
Total work (kJ)	41.2 (14.8–96.4)	46.1 (14.7–96.4)	0.88
Average exercise RQ	0.93 (0.87–1.0)	0.90 (0.84–0.95)	0.22
5-min recovery RQ (average 1–5 min)	0.92 (0.84–1.0)	0.95 (0.90–1.01)	0.30
20-min recovery RQ (average 6–20 min)	0.87 (0.82–0.96)	0.91 (0.86–0.95)	0.22
EPOC magnitude (L O_2)	2.79 (1.14–5.24)	1.46 (0.56–2.80)	0.036
Time to resting $\dot{V}O_2$ (min)	5.9 (1.0–20.0)	4.9 (2.0–9.0)	1.0

Values are presented as mean (range).

TABLE 4. Submaximal exercise and recovery results for the adolescents with cystic fibrosis (CF) and healthy, matched controls (C) when PO was set at the same absolute level.

Table 3 provides more detailed data on submaximal exercise and recovery when relative intensity was set at 50% $V \cdot O_{2peak}$. The two groups had similar maximal heart rate, blood pressure, and RPE responses during the 20-min constant load submaximal exercise session. When both groups performed the same relative intensity, the C group maintained a higher average PO and expended more energy over the 20 min of exercise and, thus, completed significantly more work [81.7 (30.7-167.7) vs 46.6 (14.8-96.4) kJ, P = 0.039]. Although the C group had higher $V \cdot O_2$ values measured in liters per minute and milliliters per kilogram per minute, the differences were not significant (P = 0.13 and 0.49, respectively). Although the C group maintained a higher average PO and expended more energy during exercise, the average RQ values were similar for both groups during exercise and at 5 and 20 min of recovery. The time to return to resting $V \cdot O_2$ values was also similar for the two groups. Interestingly, although the PO for the submaximal exercise session was chosen to elicit O_2 consumption values equal to 50% of $V \cdot O_{2peak}$ in both groups, the CF group worked at slightly higher average values [60.3% (50.1-69.4%) vs 53.2% (40.0-67.5%), P = 0.12].

When PO was set at the same absolute levels (Table 4), CF individuals required higher heart rates and relative O_2 consumption to complete the submaximal exercise session. Total work completed was similar for the CF [41.2 (14.8-96.4) kJ] and C [46.1 (14.7-96.4) kJ] ($P = 0.88$), but average O_2 consumption was less for the C group to complete the same absolute PO ($P = 0.016$). Although the CF subjects worked at a greater percent of their $V{\cdot}O_{2peak}$ [66.8% (50.1-69.4%) vs 42.7% (19.1-68.3%), $P = 0.016$], the CF and the C groups had similar RPE, BP, total exercise EE, and RQ values, and there was no difference in the time to reach resting O_2 consumption.

Ventilatory equivalents for O_2 and CO_2 during the first five stages of the maximal exercise are shown in Figure 2. $V{\cdot}E/V{\cdot}O_2$ was significantly greater in the CF group during stage 4 only [36.1 (25.7-46.0) vs 29.9 (22.8-35.3) for CF and C, respectively, $P = 0.031$], and $V{\cdot}E/V{\cdot}CO_2$ was significantly greater in the CF group during stage 2 only [39.0 (30.5-48.8) vs 34.2 (27.9-43.7) for CF and C, respectively, $P = 0.018$]. Figure 3 shows the ventilatory equivalents for O_2 and CO_2 during the relative submaximal exercise bout. The $V{\cdot}E/V{\cdot}O_2$ was not different between the two groups, and $V{\cdot}E/V{\cdot}CO_2$ was significantly greater in the CF group only for the first minute of exercise [36.9 (27.6-42.6) vs 31.3 (26.5-38.0) for CF and C, respectively, $P = 0.031$].

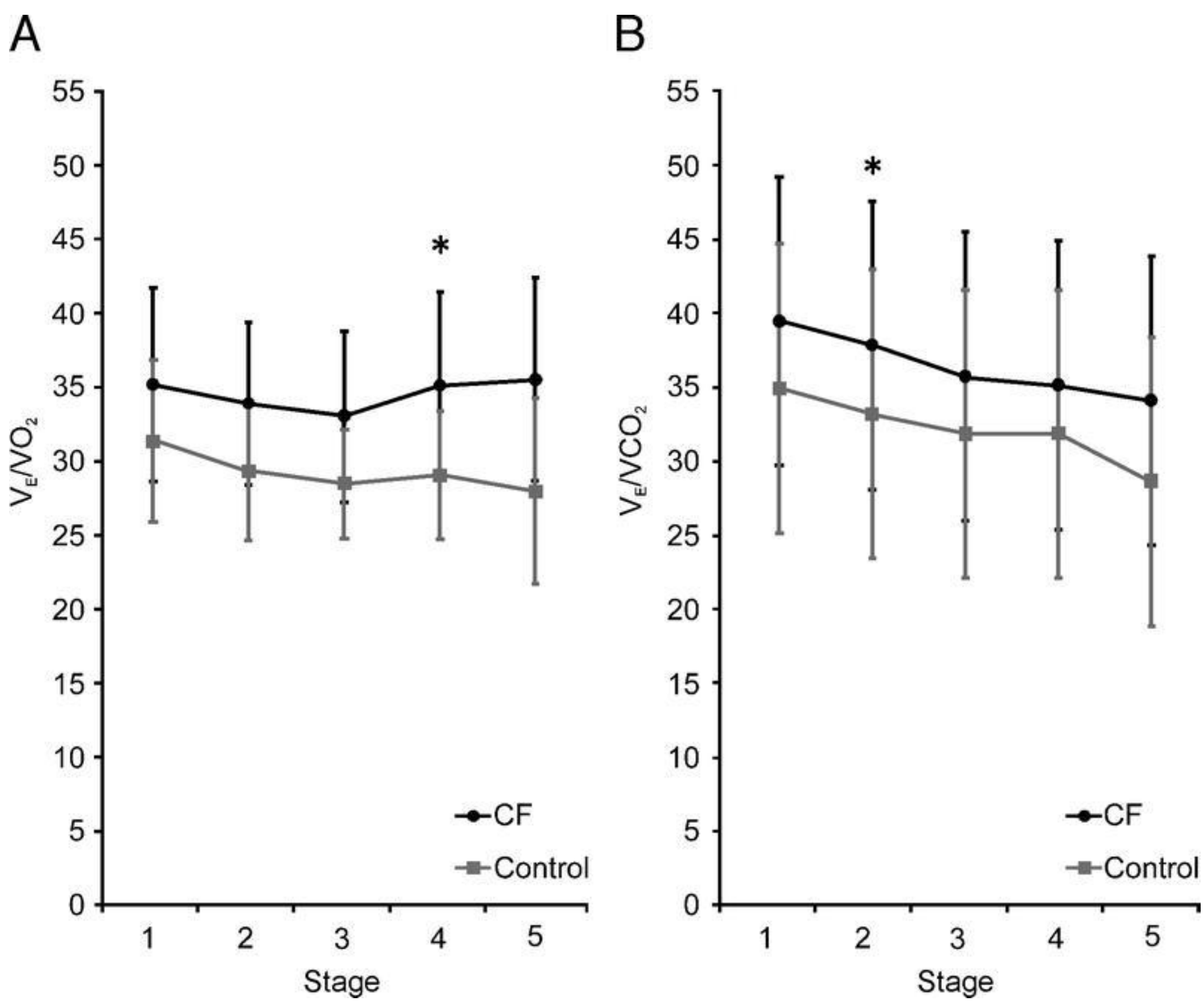

FIGURE 2-Ventilatory equivalents for O_2 calculated as V·E/V·O_2 (A) and CO_2 calculated as V·E/V·CO_2 (B) during the first five stages of the V·O_{2peak} test for CF (solid circles) and controls (solid squares). Values are presented as mean ± SD. *P < 0.05.

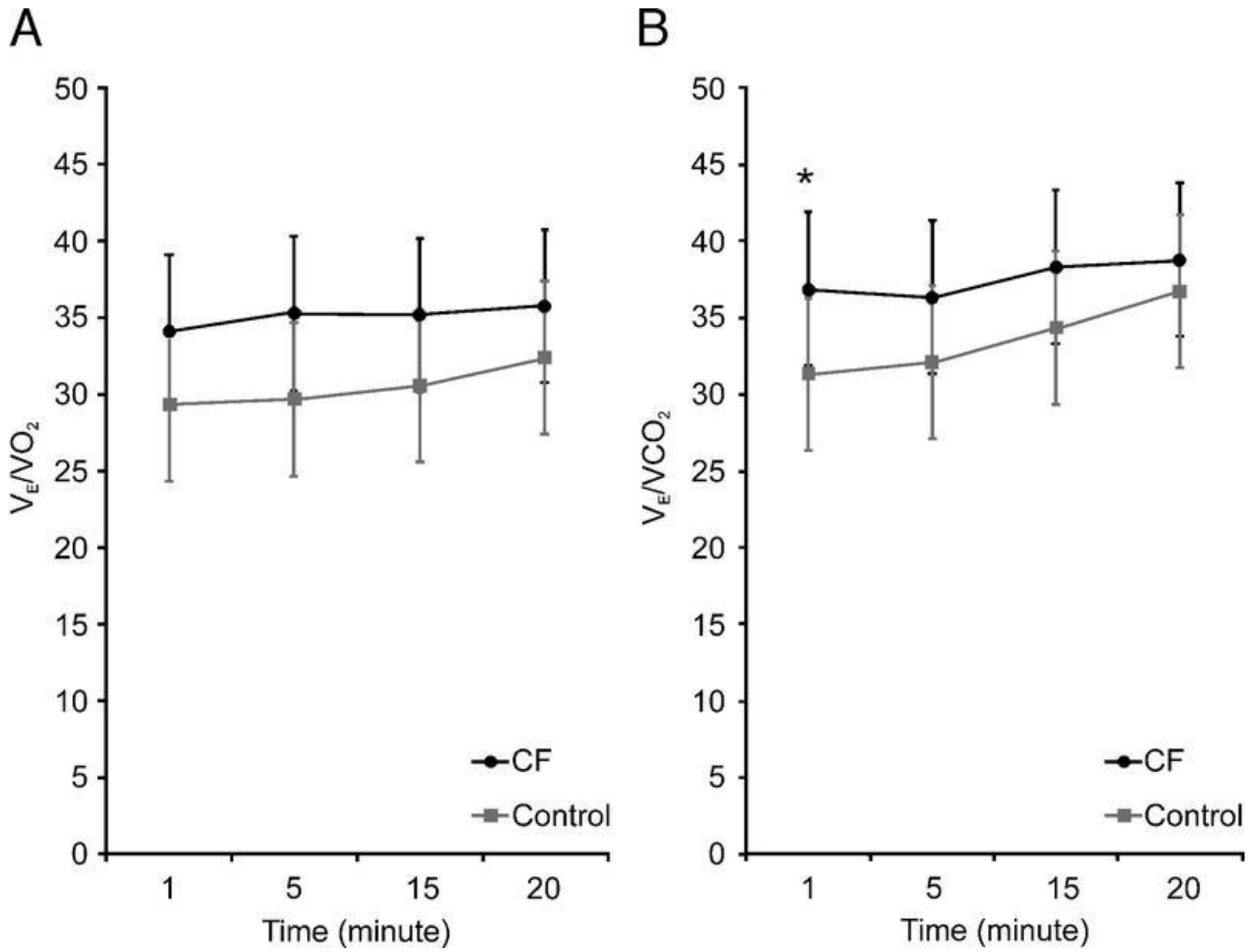

FIGURE 3-Ventilatory equivalents for O_2 calculated as V·E/V·O_2 (A) and CO_2 calculated as V·E/V·CO_2 (B) for CF (solid circles) and controls (solid squares) during the relative submaximal constant load exercise test. Values are presented as mean ± SD. *P < 0.05.

DISCUSSION

This study found that 1) similar RQ values and, therefore, similar CHO and fat utilization occur during maximal exercise and recovery in C and CF adolescents despite differences in the maximal workload attained, the total work completed, the total energy expended, or the V·O_{2peak} value attained; 2) short duration submaximal aerobic exercise (20 min on a cycle ergometer) at the same relative intensity (50% V·O_{2peak}) resulted in similar RQ values (similar CHO and fat utilization) during exercise and recovery for both CF and C; and 3) during short duration submaximal aerobic exercise (20 min on a cycle ergometer), at the same absolute power output (PO) as C adolescents, CF individuals had higher heart rates, higher V·O_2 values (mL·kg^{-1}·min^{-1}) during exercise, and higher excess postexercise oxygen consumption (EPOC) despite similar exercise EE and CHO and fat utilization during exercise and recovery.

Similar to Ward et al. (48), our study indicates that CHO and fat utilization and EE are similar during exercise in CF patients with mild to moderate disease and healthy, matched control adolescents. During maximal exercise, submaximal exercise at a fixed relative intensity, and submaximal exercise at a fixed absolute PO, the CF and the C groups had similar RQ values and, thus, similar CHO and fat utilization. Although Ward et al. (48) did not specifically measure EPOC, they found significantly higher EE ($kJ \cdot min^{-1}$) after a submaximal exercise session at a fixed absolute PO in CF adults compared with control subjects. We also noted significantly greater EPOC during recovery from submaximal exercise at a fixed absolute workload in the CF adolescents compared with the C group. The magnitude of EPOC measured in our study was similar to that reported by Short and Sedlock (40) after submaximal exercise bouts at a fixed absolute intensity in trained versus untrained individuals. In the current study, CF and C individuals had similar average PO, total exercise EE, and total work during the exercise bout with a fixed absolute intensity, but CF individuals had higher heart rates, had average $V \cdot O_2$ ($mL \cdot kg^{-1} \cdot min^{-1}$), and were working at a higher percentage of their $V \cdot O_{2peak}$. Although the magnitude of EPOC is determined by many factors, elevation in heart rate is a known contributor (20).

Spicher et al. (41) reported significantly greater RQ values and, thus, higher CHO utilization during submaximal exercise at set workloads in CF subjects (age 8-24) than in controls. However, these results must be interpreted with caution because maximal exercise testing was not completed and the intensity of effort for each group could not be determined. Intensity of effort is known to influence macronutrient utilization: increasing intensity (% $V \cdot O_{2peak}$) results in greater CHO utilization (6). When individuals are given an identical exercise task (workload or PO is set at a constant level), the task will represent varying levels of exercise intensity for the individuals, and this difference will greatly influence macronutrient substrate utilization. Results from the current study clearly demonstrate this. When both groups completed the same absolute PO for 20 min, the effort was significantly less strenuous for the C group (~47% $V \cdot O_{2peak}$) than the CF group (~60% $V \cdot O_{2peak}$). Although the CF group had a slightly higher RQ (0.93 vs 0.90), the difference was not significant. A more taxing workload or a longer exercise bout might have resulted in significantly greater RQ values simply due to the increased intensity of effort in the CF group.

We also had both groups complete a submaximal exercise session at the same relative intensity (50% $V \cdot O_{2peak}$) to allow us to directly compare macronutrient substrate utilization at the same intensity of effort. In this situation, RQ values were almost identical for the two groups although the C group had higher average PO and greater exercise EE. Although exercise at the same relative intensity allows unbiased comparison of RQ, it does not represent a free-living situation. To prescribe exercise at a relative intensity, a measure or prediction of maximal O_2 consumption must be done. Subjects must also be provided with a corresponding heart rate range and an accurate way to measure heart rate to ensure they are exercising at the proper intensity level. A controlled, clinical exercise intervention is the ideal situation, but it is not realistic for most adolescents. Instead they are asked to "keep up with their peers" on the soccer field, the basketball court, or the track. They must perform at the same absolute workload to be competitive with their peers.

To investigate the possible role of ventilation in limiting the exercise performance of CF individuals in the current study, we calculated the breathing reserve index at maximal exercise (BRI_{max}) and the ventilatory equivalents for O_2 ($V{\cdot}E/V{\cdot}O_2$) and CO_2 ($V{\cdot}E/V{\cdot}CO_2$). In general, the maximal exercise ventilation (V·E) represents 50-80% of MVV, and most of our subjects fell within this range. A high BRI_{max} suggests a low breathing reserve and indicates that exercise capacity may be limited by ventilatory capacity (37,49). In the current study, ventilation does not appear to have limited maximal exercise performance for most subjects because BRI_{max} was within the normal range. During maximal exercise testing, both the CF and the C group had similar responses for ventilatory equivalents, but as noted in a previous study (14), the values were greater in the CF patients. As outlined by Wasserman et al. (49), $V{\cdot}E/V{\cdot}CO_2$ decreased during the first few stages and $V{\cdot}E/V{\cdot}O_2$ remained stable and then increased (Fig. 2), a specific demonstration that the anaerobic threshold has been passed. This occurs earlier in the CF group compared with the C group. We also calculated the ventilatory equivalents during the relative submaximal exercise session (50% $V{\cdot}O_{2peak}$) and observed that the values were greater for the CF group compared with the C group at all time points, but this difference was significant only for $V{\cdot}E/V{\cdot}CO_2$ during the first minute of the constant load exercise test. Interestingly, the ventilation and the $V{\cdot}CO_2$ values were significantly greater in the C group during this first minute, but the ratio was significantly lower in the C group. We speculate that this finding is related to slower O_2 uptake kinetics that has been noted in CF subjects during activity transitions (12).

Some studies have reported increased REE in CF patients (1,11,33,39,41,46,47), whereas others have not (14,19,35,48). There are many possible reasons for these inconsistent results, including whether the groups were matched, what criteria were used to match groups, and how severe the disease was in CF patients. In the present study, we did not find differences in REE, even when we controlled for FFM [REE/FFM ($P = 0.139$) or REE/[square root]FFM ($P = 0.441$); data not reported for these variables]. This is probably because patients in the study had only mild to moderate CF (FEV_1% was >40% predicted) and many had PFT that were only slightly lower than normal. Thus, the metabolic cost of ventilation for these individuals was probably not significantly elevated above that for the C group. In addition, we matched our subjects on many variables, including BMI, age, gender, and pubertal stage. The significance of pubertal stage matching should not be underestimated in this population because similar biological age does not always equate to similar developmental stage.

In our study, the $V{\cdot}O_{2peak}$ values were approximately 10 $mL{\cdot}kg^{-1}{\cdot}min^{-1}$ lower in the CF group than in the C group, indicating lower levels of aerobic fitness in the CF group. The maximal O_2 consumption values obtained by our C group were similar to the values published by Nixon and Orenstein (27), and the values obtained by our group of CF patients were slightly below the average reported by some investigators (28,31) but similar to the average reported by others (17,38). Several studies have shown that peak O_2 uptake is related to both FEV_1% predicted (28) and mortality in individuals with CF (23,28,31,42). Only one of our CF subjects had a $V{\cdot}O_{2peak}$ value >45 $mL{\cdot}kg^{-1}{\cdot}min^{-1}$ and six subjects had $V{\cdot}O_{2peak}$ values <32 $mL{\cdot}kg^{-1}{\cdot}min^{-1}$. Interestingly, several studies (17,31) have shown that CF individuals with similar disease severity (as assessed by FEV_1) have different prospects of survival depending on their $V{\cdot}O_{2peak}$ values. Thus, the $V{\cdot}O_{2peak}$ values of six of our CF patients indicate a less than favorable survival outcome (31). Although there is a learning effect in the measurement of $V{\cdot}O_{2peak}$ (31) and subject effort is crucial for accurate assessment of $V{\cdot}O_{2peak}$, it is unlikely that $V{\cdot}O_{2peak}$ values would differ extraordinarily after multiple attempts. In fact, in the current study, RQ values during maximal testing were greater than 1.1 in both groups, a classic indicator of ma ximal effort. It is important to remember, however, that effort is only one of many factors that can influence the measurement of $\dot{V}O_{2peak}$. Genetics plays a substantial role in determining $\dot{V}O_{2peak}$ (3), and the genes that result in attainment of higher $\dot{V}O_{2peak}$ values may also confer a survival advantage in CF (31). In fact, several studies have indicated that exercise performance may be limited in CF patients due to secondary pathological changes in skeletal muscle (8), and these have been shown to be independent of muscle size (25).

In the current study, we used submaximal constant load exercise testing because it allowed us to address the issues of substrate utilization during an activity that was fairly representative of activities of daily living (22,26). In addition, submaximal constant load exercise testing may have other advantages for CF patients. Submaximal exercise responses are less reliant on genetics than $\dot{V}O_{2peak}$, allow assessment of factors that limit exercise performance on a day-to-day basis (26), may be less risky for CF patients than maximal exercise tests, and are an excellent indicator of changes in fitness level with training (22). However, caution is necessary in selecting the type of submaximal exercise test that is used because Narang et al. (26) showed that short sessions of submaximal exercise, such as the 3-min step test, missed important information that might have been revealed by more complex exercise tests. More research is needed to explicate whether performance on a submaximal constant load exercise test is predictive of survival or linked to mortality in patients with CF.

The current study suggests that adolescent CF patients with mild to moderate disease who are habitually participating in PA may not require adjustments in their macronutrient intake ratio (CHO vs fat) because their RQ values were similar to control subjects during maximal and submaximal exercise and recovery. Although REE and exercise EE were not significantly elevated in CF individuals in the current study, the submaximal exercise sessions were of relatively short duration (20 min). Increased total caloric intake may be preferential for individuals with CF who are habitually participating in PA that requires high-intensity work or relatively long durations (45-60 min), which may result in significant EPOC. A recent study by Johnson et al. (14) provided CF patients with fat or CHO supplements equaling 50% of their REE during a 6-wk supervised exercise program in an effort to manipulate EE. The authors did not directly measure activity, all the CF patients received supplementation, and no postintervention testing was done to assess improvements in physical capacity (14), so it is difficult to discern the role of supplementation for increasing participation in PA for CF patients. Clearly, more work is needed in this area.

In summary, although recent data show that lung function is preserved in CF patients who participate in regular exercise (22,29), no studies have directly tested the hypothesis that patients with CF who remain physically active succeed in delaying the onset of respiratory failure (31). Any intervention that improves or at the very least preserves lung function over the long term has important implications for disease management (22,29), and exercise programs appear to fulfill this role. What remains to be elucidated are the factors that need to be addressed to provide the best clinical support for individuals with CF as they pursue increased PA.

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REFERENCES

1. Allen JR, McCauley JC, Selby AM, et al. Differences in resting energy expenditure between male and female children with cystic fibrosis. J Pediatr. 2003;142:15-9.
2. Barker M, Hebestreit A, Gruber W, Hebestreit H. Exercise testing and training in German CF centers. Pediatr Pulmonol. 2004;37:351-5.
3. Bouchard C, Dionne F, Simoneau JA, Boulay MR. Genetics of aerobic and anaerobic performances. Exerc Sport Sci Rev. 1992;20:27-58.
4. Boucher G, Lands L, Hay J, Hornby L. Activity levels and the relationship to lung function and nutritional status in children with cystic fibrosis. Am J Phys Med Rehabil. 1997;76:311-5.
5. Britto MT, Garrett JM, Konrad TR, Majure JM, Leigh MW. Comparison of physical activity in adolescents with cystic fibrosis versus age-matched controls. Pediatr Pulmonol. 2000;30:86-91.
6. Brooks G, Mercier J. Balance of carbohydrate and lipid utilization during exercise: the crossover concept. J Appl Physiol. 1994;76(6):2253-61.
7. de Jong W, Grevink RG, Roorda RJ, Kaptein AA, van der Schans C. Effect of a home exercise training program in patients with cystic fibrosis. Chest. 1994;105(5):463-8.
8. de Meer K, Jeneson JA, Gulmans VAM, van der Laag J, Berger R. Efficiency of oxidative work performance of skeletal muscle in patients with cystic fibrosis. Thorax. 1995;50:980-3.
9. Dodd JD, Barry SC, Gallagher CG. Respiratory factors do not limit maximal symptom-limited exercise in patients with mild cystic fibrosis lung disease. Respir Physiol Neurobiol. 2006;152:176-85.
10. Godfrey S. Exercise Training in Children. London: W.B. Saunders Co. Ltd.; 1974. p. 30.
11. Grunow J, Azcue M, Berall G, Pencharz P. Energy expenditure in cystic fibrosis during activities of daily living. J Pediatr. 1993;122(2):243-6.
12. Hebestreit H, Hebestreit A, Trusen A, Hughson RL. Oxygen uptake kinetics are slowed in cystic fibrosis. Med Sci Sports Exerc. 2005;37(1):10-7.
13. Javadpour SM, Selvadurai HC, Wilkes DL, Schneiderman-Walker J, Coates AL. Does carbon dioxide retention during exercise predict a more rapid decline in FEV_1 in cystic fibrosis? Arch Dis Child. 2005;90:792-5.
14. Johnson MR, Ferkol TW, Shepherd RW. Energy cost of activity and exercise in children and adolescents with cystic fibrosis. J Cyst Fibros. 2006;5(1):53-8.
15. Keochkerian D, Chlif M, Delanaud S, Gauthier R, Maingourd Y, Ahmaidi S. Timing and driving components of the breathing strategy in children with cystic fibrosis during exercise. Pediatr Pulmonol. 2005;40:449-56.

16. Lees CM, Smyth RL. The current management of cystic fibrosis. Int J Clin Pract. 2000;54(3):171-9.
17. Loutzenhiser JK, Clark R. Physical activity and exercise in children with cystic fibrosis. J Pediatr Nurs. 1993;8(2):112-9.
18. Marcotte JE, Grisdale RK, Levison H, Coates AL, Canny GJ. Multiple factors limit exercise capacity in cystic fibrosis. Pediatr Pulmonol. 1986;9:974-81. 19. Marin V, Velandia S, Hunter B, et al. Energy expenditure, nutrition status, and body composition in children with cystic fibrosis. Nutrition. 2004;20:181-6.
20. McArdle WD, Katch FI, Katch VL. Exercise Physiology; Energy, Nutrition, & Human Performance. Baltimore (MA): Lippincott Williams & Wilkins; 2007. p. 192.
21. McIlwaine M, Davidson A. Airway clearance techniques in the treatment of cystic fibrosis. J Pediatr. 1996;2:447-51.
22. Moorcroft A, Dodd M, Morris J, Webb A. Individualised unsupervised exercise training in adults with cystic fibrosis: a 1 year randomised controlled trial. Thorax. 2004;59:1074-80.
23. Moorcroft A, Dodd M, Webb A. Exercise testing and prognosis in adult cystic fibrosis. Thorax. 1997;52:291-3.
24. Morris NM, Udry JR. Validation of a self-administered instument to assess stage of adolescent development. J Youth Adolesc. 1980;9(3):271-80.
25. Moser C, Tirakitsoontorn P, Nussbaum E, Newcomb R, Cooper DM. Muscle size and cardiorespiratory response to exercise in cystic fibrosis. Am J Respir Crit Care Med. 2000;162:1823-7.
26. Narang I, Pike S, Rosenthal M, Balfour-Lynn I, Bush A. Three-minute step test to assess exercise capacity in children with cystic fibrosis with mild lung disease. Pediatr Pulmonol. 2003;35:108-13.
27. Nixon PA, Orenstein DM. Exercise testing in children. Pediatr Pulmonol. 1988;5:107-22.
28. Nixon PA, Orenstein DM, Kelsey SF, Doershuk CF. The prognostic value of exercise testing in patients with cystic fibrosis. N Engl J Med. 1992;327(25):1785-8.
29. Orenstein D, Higgins L. Update on the role of exercise in cystic fibrosis. Curr Opin Pulm Med. 2005;11:519-23.
30. Orenstein DM, Hovell MF, Mulvihill M, et al. Strength vs aerobic training in children with cystic fibrosis. Chest. 2004;126:1204-14.
31. Pianosi P, LeBlanc J, Almudevar A. Peak oxygen uptake and mortality in children with cystic fibrosis. Thorax. 2005;60:50-4.
32. Reilly J, Edwards C, Weaver L. Malnutrition in children with cystic fibrosis: the energy-balance equation. J Pediatr Gastroenterol Nutr. 1997;25:127-36.
33. Richards ML, Davies PSW, Bell SC. Energy cost of physical activity in cystic fibrosis. Eur J Clin Nutr. 2001;55:690-7.
34. Schneiderman-Walkers J, Pollock SL, Corey M, et al. A randomized controlled trial of a 3-year home exercise program in cystic fibrosis. J Pediatr. 2000;136:304-10.
35. Selvadurai HC, Allen JC, Sachinwalla T, Macauley J, Blimkie CJ, Van Asperen PP. Muscle function and resting energy expenditure in female athletes with cystic fibrosis. Am J Respir Crit Care Med. 2003;168:1476-80.
36. Selvadurai HC, Blimkie CJ, Cooper PJ, Mellis CM, Van Asperen PP. Gender differences in habitual activity in children with cystic fibrosis. Arch Dis Child. 2004;89:928-33.

37. Sexauer WJ, Cheng H-K, Fiel SB. Utility of the breathing reserve index at the anaerobic threshold in determining ventilatory-limited exercise in adult cystic fibrosis patients. Chest. 2003;124(4):1469-75.
38. Shah AR, Gozal D, Keens TG. Determinants of aerobic and anaerobic exercise performance in cystic fibrosis. Am J Respir Crit Care Med. 1998;157:1145-50.
39. Shepherd RW, Greer RM, McNaughton SA, Wotton M, Cleghorn GJ. Energy expenditure and the body cell mass in cystic fibrosis. Nutrition. 2001;17:22-5.
40. Short KR, Sedlock DA. Excess postexercise oxygen consumption and recovery rate in trained and untrained subjects. J Appl Physiol. 1997;83(1):153-9.
41. Spicher V, Roulet M, Schutz Y. Assessment of total energy expenditure in free-living patients with cystic fibrosis. J Pediatr. 1991;118:865-72.
42. Stanghelle JK, Michalsen H, Skyberg D. Five-year follow-up of pulmonary function and peak oxygen uptake in 16-year-old boys with cystic fibrosis, with special regard to the influence of regular physical exercise. Int J Sports Med. 1988;9(suppl.):19-24.
43. Suri R, Metcalfe C, Wallis C, Bush A. Assessing the usefulness of outcomes measured in a cystic fibrosis treatment trial. Respir Med. 2007;101:254-60.
44. Tantisira KC, Systrom DM, Ginns LC. An elevated breathing reserve index at the lactate threshold is a predictor of mortality in patients with cystic fibrosis awaiting lung transplantation. Am J Respir Crit Care Med. 2002;165:1626-33.
45. Tirakitsoontorn P, Nussbaum E, Moser C, Hill M, Cooper D. Fitness, acute exercise and anabolic and catabolic mediators in cystic fibrosis. Am J Respir Crit Care Med. 2001;164:1432-7.
46. Tomezsko JL, Stallings VA, Kawchak DA, Goin JE, Diamond G, Scanlin TF. Energy expenditure and genotype of children with cystic fibrosis. Pediatr Res. 1994;35(4):451-60.
47. Vaisman N, Pencharz PB, Corey M, Canny GJ, Hahn E. Energy expenditure of patients with cystic fibrosis. J Pediatr. 1987;111:496-500.
48. Ward SA, Tomezsko JL, Holsclaw DS, Paolone AM. Energy expenditure and substrate utilization in adutls with cystic fibrosis and diabetes mellitus. Am J Clin Nutr. 1999;69:913-9.
49. Wasserman K, Hansen JE, Sue DY, Stringer WW, Whipp BJ. Principles of Exercise Testing and Interpretation; Including Pathophysiology & Clinical Applications. Philadelphia (PA): Lippincott Williams & Wilkins; 2005. p. 89-90; 172-4.
50. Weston A, Petrosa R, Pate R. Validation of an instrument for measurement of physical activity in youth. Med Sci Sports Exerc. 1997;29(1):138-43.

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