Energy expenditure and substrate utilization in adults with cystic fibrosis and diabetes mellitus$^{1,2}$

Sheila A Ward, Jean L Tomezsko, Douglas S Holsclaw, and Albert M Paolone

ABSTRACT

Background: The onset of cystic fibrosis–related diabetes mellitus (CFDM) is often associated with a decline in clinical and nutritional status.

Objective: The purpose of this study was to characterize energy expenditure (EE) and substrate utilization during rest, exercise, and recovery from exercise in patients with CF diagnosed with diabetes mellitus.

Design: EE, substrate utilization, minute ventilation, tidal volume, and respiratory rate were calculated by indirect calorimetry during rest; a 30-min, low-to-medium-intensity exercise bout on a treadmill; and a 45-min postexercise recovery period (in reclining position) in 10 CF, 7 CFDM, and 10 control subjects between 18 and 45 y of age.

Results: In all 3 periods, minute ventilation was higher in the CF and CFDM groups than in the control subjects ($P < 0.01$). During rest and exercise, the CF and CFDM groups maintained EE values at the high end of the normal range of the control subjects. However, during recovery, EE was higher in the CF and CFDM groups than in the control group ($P < 0.01$).

Conclusions: EE may be higher than usual for the patients with CF and CFDM during periods of recovery from mild exercise or activity because of increased work of breathing consistent with higher ventilatory requirements. This information may be useful for patients receiving nutritional counseling who may choose to exercise regularly, but are concerned about possible weight loss. Am J Clin Nutr 1999;69:913–9.

KEY WORDS Cystic fibrosis, diabetes mellitus, dietary intake, energy expenditure, oxygen consumption, exercise, adults, humans

INTRODUCTION

Cystic fibrosis (CF) is the most common, severe genetic disorder in the United States. A dramatically improved median age of survival (29 y) has been reported in recent years (1) because of advances in a variety of treatment regimens. In addition to improved antibiotics and respiratory medications, nutritional care has improved. In conjunction with pancreatic enzyme supplements, a high-energy diet with unrestricted fat has greatly aided the prevention of growth failure and malnutrition, both of which have been associated with decreased quality of life and survival (2). Management has become even more complicated with the development of impaired glucose tolerance (26–75% of patients) and diabetes mellitus (DM) (2.5–12%) probably because of the destruction of pancreatic tissue. The mean age of diagnosis for overt diabetes, 19–20 y, is remarkably consistent and the age of 20 y seems to mark a point of rapid decline in the survival of patients with CF-related DM (CFDM), with <25% reaching the age of 30 y compared with 60% of the nondiabetic patients with CF (3). Other studies have shown conflicting results with regard to survival, pulmonary function, and nutritional status (4–6). The Cystic Fibrosis Foundation has outlined guidelines for CFDM and stressed the complexity of treatment of a second chronic illness (7).

The struggle to maintain good nutritional status continues throughout life. Causes of malnutrition and growth failure in CF are an inadequate energy intake, some malabsorption despite pancreatic enzyme supplementation, and increased energy expenditure (EE). EE is the energy used for work and heat produced by the body to sustain life processes and activity. Increased EE in patients with CF results from respiratory infections, inflammation, fever, theorized increased work of breathing, medications, and possibly the basic genetic defect itself. Loss of glucose energy in the urine, altered metabolism, along with a possible increased EE can easily put patients with CF and DM in negative energy balance (8).

This study was undertaken to provide a better understanding of CFDM and its role in nutritional status. The purpose of this study was to characterize the EE and pattern of substrate utilization of stable ambulatory adult patients with CF and CFDM during rest, exercise, and recovery from exercise and to examine body composition, ventilatory requirements, selected substrates, and nutrient intakes.
SUBJECTS AND METHODS

Subjects

A total of 27 men and women aged 18–45 y were recruited and represented 3 study groups. The subjects with CF were recruited from the CF patient populations at Hahnemann University Hospital, the Medical College of Pennsylvania, and the University of Pennsylvania Medical Center (all in Philadelphia). CF patients were grouped according to those without DM (CF group, n = 3 women and 7 men) and those with DM (CFDM group, n = 2 women and 5 men). All patients were clinically stable. No patient with CF was allowed to participate if they were severely malnourished (≤75% of ideal body weight), receiving supplemental oxygen during the daytime, or taking thyroid or cardiac medication.

Eight of the 10 subjects in the CF group and all the CFDM patients were pancreatic insufficient. Eight of the 10 subjects in the CF group were using bronchodilators, 1 subject was not, and 1 subject’s bronchodilator status was unknown. All CFDM subjects were using bronchodilators. However, on the morning of the study, use of bronchodilators and all other medications was not allowed. Of the 10 patients in the CF group, 3 were ΔF508 homozygous, 4 were ΔF508 heterozygous (other mutations were S549N and W1282X with 2 genes unidentified), 2 were W1282X/3849 + 10, and 1 was G551D with an unidentified gene. Of the 7 patients in the CFDM group, 1 was ΔF508 homozygous and 5 were ΔF508 heterozygous (other genes were 621+1 and R553X with 2 genes unidentified; one was 441 with an unidentified gene.

Control subjects (n = 5 women and 5 men) were healthy with no known medical conditions and were recruited from hospital and community sources. The control group was age- and weight-matched to the CF and CFDM groups, but not individually so. The duration of diabetes in the CFDM group was 6 ± 3.9 y and the CFDM group was significantly older than the control group (P < 0.03). No persons known to be alcohol or drug addicted or febrile the morning of the study were allowed to participate. The study was conducted at Hahnemann University Hospital. All subjects gave written consent and the protocol was approved by the Committee on Human Subjects, Hahnemann University Hospital.

Study design

The CF, CFDM, and control groups were studied in the early morning after a 12-h overnight fast. Subjects in the CFDM group were studied 8–10 h after their last regularly scheduled meal and evening medication administration. Water was allowed and encouraged during the fasting period and all medications and regular therapies, including chest physiotherapy and bronchodilators, were withheld. Screening blood glucose tests were performed and temperatures were taken on the morning of the study. Patients in the CFDM group were also screened after the exercise and recovery periods. Measurements were taken for weight, height, body composition, and lung status. Subjects reclined quietly and rested for 30 min before baseline measurements of EE, substrate utilization, ventilatory indexes, and selected blood indexes were made; the same measurements were made during the exercise and recovery periods. No medications or therapies, such as bronchodilators, were administered after the exercise period. For patients in the CFDM group, poststudy medication was adjusted and given with the poststudy meal immediately after the study was completed.

Physical characteristics and body composition

Measurements of weight, height, skinfold thicknesses (biceps, triceps, subscapular, and suprailiac with Lange calipers; Cambridge Scientific Instruments, Cambridge, MD), and midarm circumference were made in triplicate by one observer (SAW). Body density (9); percentage body fat, fat mass, and fat-free mass (FFM; 10); and midarm muscle circumference (11) were also measured. Percentage ideal body weight (12), body surface area (by nomogram), and body mass index (13) were calculated.

Ventilatory indexes

Pulmonary function tests were performed with a Spiro Analyzer ST-90 (Futuremed, Deer Park, NY). The forced vital capacity (FVC) and forced expiratory volume in 1 s (FEV1), which evaluate the resistance properties of the airways and the strength of the expiratory muscles, were determined (14). Minute ventilation (V̇E), tidal volume (V̇T), oxygen consumption (VO2), and respiratory rate (RR) were also measured during the same time periods and with the same procedure as described for EE.

Blood analyses

Approximately 16 mL blood was drawn from a catheter inserted into the left brachial vein at the end of the rest, exercise, and postexercise recovery periods. After centrifugation at 4°C for 10–15 min at 2739–5590 × g (3500–5000 rpm), all blood samples were separated, stored at −40°C, and analyzed according to hospital laboratory procedures at Hahnemann University Hospital (glucose, triacylglycerol, and urea) or the General Clinical Research Center at Temple University (catecholamines, glucagon, and insulin).

Blood drawn for triacylglycerol and urea measurements was placed in a heparin-containing tube, shaken, and placed on ice until centrifuged and analyzed with the glycerol phosphate oxidase enzymatic (Boehringer Mannheim, Mannheim, Germany) and urease method (Boehringer Mannheim), respectively. Blood samples for glucagon measurements were placed in refrigerated tubes containing 0.2 mL Trasylol (Bayer, West Haven, CT), shaken, and placed on ice until centrifuged and analyzed by radioimmunoassay. Blood samples for catecholamine analyses were placed in refrigerated Amersham tubes (Piscataway, NJ), shaken, placed on ice, centrifuged within 15 min, and analyzed (15). Blood samples for insulin measurements were clotted at room temperature for 30 min, centrifuged, and analyzed by the standard double-antibody immunoassay (Pharmacia Diagnostics, Uppsala, Sweden). Blood samples for glucose measurement were clotted at room temperature for 15–20 min, centrifuged, and analyzed by the hexokinase method (Boehringer Mannheim).

Dietary intake

Nutrient intakes were derived from a self-reported dietary record maintained by the subjects for 3 d before the study day after they had been given verbal and written instructions. Subjects weighed, measured, and recorded food intakes. All enzyme supplements for each meal were also recorded. Energy intake and dietary analyses were conducted by using a computerized program, NUTRITIONIST III (Salem, OR).

Energy expenditure and substrate utilization

EE and substrate (carbohydrate, fat, and protein) utilization were calculated from the amount of oxygen utilized and carbon dioxide produced during 3 time periods on the same day by
TABLE 1
Physical characteristics, body-composition, resting energy expenditure (REE), and lung function values for the 3 study groups

<table>
<thead>
<tr>
<th>Variable</th>
<th>CF group (n = 7 M and 3 F)</th>
<th>CFDM group (n = 5 M and 2 F)</th>
<th>Control group (n = 5 M and 5 F)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>31.1 ± 7.30</td>
<td>33.1 ± 1.76&lt;sup&gt;2&lt;/sup&gt;</td>
<td>25.7 ± 4.00</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>63.8 ± 8.46</td>
<td>63.0 ± 12.10</td>
<td>61.8 ± 11.37</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>172.4 ± 10.00</td>
<td>169.0 ± 6.23</td>
<td>167.9 ± 9.51</td>
</tr>
<tr>
<td>Percentage of IBW (%)</td>
<td>98.5 ± 15.04</td>
<td>104.9 ± 14.09</td>
<td>102.7 ± 11.20</td>
</tr>
<tr>
<td>Percentage body fat (%)</td>
<td>19.6 ± 8.02</td>
<td>20.4 ± 6.00</td>
<td>23.1 ± 6.53</td>
</tr>
<tr>
<td>Fat-free mass (kg)</td>
<td>51.5 ± 9.87</td>
<td>50.0 ± 9.25</td>
<td>47.9 ± 11.36</td>
</tr>
<tr>
<td>Fat mass (kg)</td>
<td>12.2 ± 4.40</td>
<td>13.0 ± 4.77</td>
<td>13.9 ± 3.19</td>
</tr>
<tr>
<td>Body mass index</td>
<td>21.4 ± 1.96</td>
<td>21.9 ± 3.29</td>
<td>22.0 ± 2.21</td>
</tr>
<tr>
<td>Body surface area (m&lt;sup&gt;2&lt;/sup&gt;)</td>
<td>1.75 ± 0.16</td>
<td>1.71 ± 0.18</td>
<td>1.70 ± 0.20</td>
</tr>
<tr>
<td>Skinfold-thickness sum (mm)</td>
<td>42.4 ± 16.94</td>
<td>45.9 ± 16.49</td>
<td>48.2 ± 12.08</td>
</tr>
<tr>
<td>REE (kJ/d)</td>
<td>6774.3 ± 1077.80</td>
<td>6957.6 ± 1459.80</td>
<td>6083.5 ± 1155.62</td>
</tr>
<tr>
<td>(kJ · kg body wt&lt;sup&gt;−1&lt;/sup&gt; · d&lt;sup&gt;−1&lt;/sup&gt;)</td>
<td>107.1 ± 17.57</td>
<td>112.5 ± 24.69</td>
<td>98.7 ± 9.62</td>
</tr>
<tr>
<td>(kJ · kg FFM&lt;sup&gt;−1&lt;/sup&gt; · d&lt;sup&gt;−1&lt;/sup&gt;)</td>
<td>134.7 ± 28.03</td>
<td>141.0 ± 26.36</td>
<td>129.3 ± 15.48</td>
</tr>
<tr>
<td>Predicted REE (kJ)</td>
<td>6572.6 ± 830.11</td>
<td>6391.9 ± 817.97</td>
<td>6428.3 ± 963.16</td>
</tr>
<tr>
<td>Percentage of predicted REE (kJ)</td>
<td>104.0 ± 17.32</td>
<td>109.2 ± 20.15</td>
<td>94.4 ± 7.95</td>
</tr>
<tr>
<td>FEV&lt;sub&gt;1&lt;/sub&gt; (% of predicted)</td>
<td>45.7 ± 15.60</td>
<td>50.3 ± 22.20</td>
<td>95.5 ± 13.70&lt;sup&gt;3&lt;/sup&gt;</td>
</tr>
<tr>
<td>FVC (% of predicted)</td>
<td>62.6 ± 12.20</td>
<td>64.9 ± 17.10</td>
<td>92.3 ± 14.00</td>
</tr>
</tbody>
</table>

<sup>1</sup>± SD. CF, cystic fibrosis; CFDM, CF plus diabetes mellitus; IBW, ideal body weight; FFM, fat-free mass; FEV<sub>1</sub>, forced expiratory volume in 1 s; FVC, forced vital capacity.

<sup>2</sup>Significantly different from the control group, P < 0.05 (post hoc Tukey-Kramer’s test).

<sup>3</sup>Significantly different from the CF and CFDM groups, P < 0.001 (post hoc Tukey-Kramer’s test).

RESULTS

The physical characteristics, body composition, baseline and REE values, and resting lung function of the 3 groups are presented in Table 1. The diabetic status of the CFDM group was as follows: stable to well controlled in 5 patients, fair in 1 patient, and unknown in 1 patient. In the CFDM group, diabetes was treated with insulin in 6 subjects and with the hypoglycemic agent Glucotrol (Pratt Pharmaceuticals, New York) in 1 subject. There were no significant differences in any of the body-composition or anthropometric data between groups. All 3 groups had good nutritional status on the basis of mean values for percentage of ideal body weight. Two subjects in the CF group had mild-to-moderate malnutrition, one subject in the CFDM group was underweight, and one control subject had mild malnutrition.

EE and substrate utilization

There was no significant difference in EE between the 3 groups during rest or exercise (Table 2). However, during recovery, EE
was significantly higher in the CF and CFDM groups than in the control group when measured as kJ/min, kJ·kg body wt⁻¹·min⁻¹, and kJ·kg FFM⁻¹·min⁻¹. There were no significant differences between the 3 groups in the incremental change of any EE variable between the rest and exercise periods and between the exercise and recovery periods. There were no significant differences in any of the substrate utilization variables between the 3 groups during exercise or recovery (Table 3). Neither the CF nor the CFDM groups reached the dietary goal of >120% of the recommended dietary allowance for energy or the suggested energy intake from fat of 35–40% (18, 19).

Ventilatory indexes

Ventilatory indexes during rest, exercise, and recovery are presented in Table 4. During rest and exercise, $V_e$, RR, and $V_O_2$ (mL·kg⁻¹·min⁻¹) were not significantly different between the 3 groups; $V_e$ was significantly higher in the CF and CFDM groups than in the control group. During recovery, $V_e$ was significantly higher in the CFDM group than in the control group ($P < 0.02$) and $V_e$ and $V_O_2$ were significantly higher in the CF and CFDM groups than in the control group ($P < 0.001$). There was no significant difference in the RR between groups.

Blood indexes

Differences in all of the blood indexes were examined between the 3 study groups. Glucagon was higher in the CFDM group (162.5 ± 3.63 ng/L) than in the control group (102.4 ± 32.3 ng/L) during rest ($P < 0.04$). Differences in all variables were also examined within each study group. Within the CF group, the blood concentration of epinephrine was significantly higher ($P < 0.01$) during exercise (3.96 ± 1.93 pmol/L) than during rest (2.22 ± 1.21 pmol/L). Norepinephrine was also significantly higher ($P < 0.01$) during exercise (0.026 ± 0.006 nmol/L) than during rest (0.015 ± 0.005 nmol/L) and recovery (0.014 ± 0.003 nmol/L). Within the CFDM group, epinephrine was significantly higher ($P < 0.01$) during exercise (5.11 ± 3.16 pmol/L) than during rest (2.97 ± 1.77 pmol/L) and recovery (3.17 ± 1.41 pmol/L), and norepinephrine was significantly higher ($P < 0.01$) during exercise (0.026 ± 0.011 nmol/L) than during rest (0.017 ± 0.005 nmol/L) and recovery (0.017 ± 0.006 nmol/L). Within the control group, epinephrine was significantly higher ($P < 0.001$) during exercise (4.57 ± 4.10 pmol/L) than during rest (2.54 ± 2.63 pmol/L) and recovery (2.08 ± 1.12 pmol/L), and norepinephrine was significantly higher ($P < 0.001$) during exercise (0.033 ± 0.019 nmol/L) than during rest (0.019 ± 0.009 nmol/L) and recovery (0.021 ± 0.009 nmol/L). There were no significant differences in triacylglycerol, urea, insulin, or glucagon across the 3 time periods (rest, exercise, and recovery) in the CF, CFDM, and control groups and no significant differences in the respiratory quotient, the nonprotein respiratory quotient, or glucose variables for the CF and control groups.

In the CFDM group, the respiratory quotient was significantly higher during exercise than during rest and recovery and significantly higher during rest than during recovery ($P < 0.04$). The nonprotein respiratory quotient was significantly higher during rest than during exercise and recovery and significantly higher during exercise than during recovery ($P < 0.03$). The blood glucose concentration was significantly higher ($P < 0.01$) during rest (8.60 ± 2.90 mmol/L) than during exercise (7.28 ± 1.61 mmol/L) and recovery (7.29 ± 2.09 mmol/L). The percentage carbohydrate utilization was significantly higher in the CF and control groups during exercise than during recovery ($P < 0.01$) and significantly higher in the CFDM group during exercise than during rest and recovery ($P < 0.01$). Within all 3 groups, the percentage of protein utilization was significantly lower during exercise than during rest and recovery ($P < 0.001$), but there were no significant differences in the percentage lipid utilization. There were also no significant differences in the incremental changes in substrate utilization between time periods (between rest and exercise and between exercise and recovery) across the 3 groups.

**DISCUSSION**

Both CF groups were well matched in lung disease severity. There were no significant differences between groups in anthropometric measures, body composition, or nutritional status. In the recovery phase, EE was significantly higher in the CF and CFDM groups than in the control group. This difference was supported by higher $V_e$, $V_V$, and $V_O_2$ values in the CF and CFDM groups than in the control group.

The respiratory muscles of patients with CF, regardless of the presence of diabetes, work harder. The respiratory muscles must generate more force to provide sufficient oxygen and gas.
Exercise and CFDM groups and the control group. This finding was con-
not reach the blood (ventilation-to-perfusion mismatch).

groups to compensate for the ventilation that is wasted because

FEV1 was compared with the following indexes: percentage ideal
value being 110%. Despite very low pulmonary function, the REE
increase as lung function declines (29). In our study, the CF and
patients varies as well (28). In CF patients, REE appears to
explain why EE variables were not significantly different
between the CF patients and the control subjects during exercise,
but were significantly different during recovery.

An elevated REE has been documented in patients with CF (21, 23–27). The REE in normal adults varies greatly, depending on
many factors, particularly the amount of metabolically active tissue.
The range of daily expended energy in severely ill non-CF patients varies as well (28). In CF patients, REE appears to
increase as lung function declines (29). In our study, the CF and
CFDM groups had subjects with predicted REE values that were
as high as 130% and 137%, respectively, whereas values in the
control group remained within normal limits, the highest predicted
value being 110%. Despite very low pulmonary function, the REE
of the CF and CFDM groups was not as high as expected. Within
each group, regression analysis of the percentage of predicted
FEV1 was compared with the following indexes: percentage ideal
body weight, percentage of predicted REE, and percentage body
fat. The only significant correlation found was between FEV1,
and percentage body fat in the CF group (r = 0.67, P < 0.05).
No adjustments were made for multiplicity of planned comparisons.

The most important function of glucagon is to increase blood
glucose concentrations, mainly via hepatic glycogenolysis and
increased hepatic gluconeogenesis. During rest, the blood
glucocan concentration of the CFDM group was significantly
increased hepatic gluconeogenesis. During rest, the blood

exchange because of airway obstruction and resistance, such as
decreased lung compliance. This additional work requires addi-
tional energy. Furthermore, \( V_E \) was higher in the CF and CFDM
groups to compensate for the ventilation that is wasted because it
never reaches the blood (ventilation-to-perfusion mismatch).

No incremental changes in EE were observed between the CF
and CFDM groups and the control group. This finding was con-
istent with that of Grunow et al (20), who found no significant
differences between CF patients and matched control subjects in
incremental increases in energy from resting to each of several activities of daily living, including 2 levels of exercise. Although
EE was higher (NS) during rest and exercise in the CF and
CFDM groups than in the control group, the CF and CFDM
groups were able to compensate and maintain EE values within
the range of those of the control group. Patients with CF and
significant pulmonary involvement have an enlarged physiologic
death space and hypoxemia at rest (21). Physiologic death space
is enlarged because any ventilation to scarred, infected, or
blocked portions of the lungs is wasted. During exercise in
persons without respiratory distress, the physiologic death space
naturally decreases (22). If, however, physiologic death space (not
measured in this study) also decreases during exercise, it might
explain why EE variables were not significantly different
between the CF patients and the control subjects during exercise,
but were significantly different during recovery.

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### Table 3
Substrate utilization in the 3 study groups during rest, exercise, and recovery

<table>
<thead>
<tr>
<th>Variable</th>
<th>CF group (n = 10)</th>
<th>CFDM group (n = 7)</th>
<th>Control group (n = 10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rest</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RQ (%)</td>
<td>0.85 ± 0.04</td>
<td>0.85 ± 0.06</td>
<td>0.83 ± 0.03</td>
</tr>
<tr>
<td>NPRQ (%)</td>
<td>0.87 ± 0.06</td>
<td>0.90 ± 0.15</td>
<td>0.83 ± 0.04</td>
</tr>
<tr>
<td>Carbohydrates (%)</td>
<td>45.0 ± 13.0</td>
<td>39.0 ± 23.3</td>
<td>38.0 ± 11.6</td>
</tr>
<tr>
<td>Lipids (%)</td>
<td>34.5 ± 16.8</td>
<td>33.5 ± 22.3</td>
<td>42.1 ± 13.3</td>
</tr>
<tr>
<td>Protein (%)</td>
<td>20.5 ± 12.0</td>
<td>27.5 ± 23.7</td>
<td>19.9 ± 7.4</td>
</tr>
<tr>
<td>Exercise</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RQ (%)</td>
<td>0.85 ± 0.05</td>
<td>0.86 ± 0.03</td>
<td>0.84 ± 0.03</td>
</tr>
<tr>
<td>NPRQ (%)</td>
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<td>0.86 ± 0.04</td>
<td>0.84 ± 0.04</td>
</tr>
<tr>
<td>Carbohydrates (%)</td>
<td>50.6 ± 17.9</td>
<td>52.7 ± 13.5</td>
<td>47.5 ± 11.3</td>
</tr>
<tr>
<td>Lipids (%)</td>
<td>43.0 ± 18.0</td>
<td>38.7 ± 9.8</td>
<td>46.7 ± 12.6</td>
</tr>
<tr>
<td>Protein (%)</td>
<td>6.4 ± 3.7</td>
<td>8.6 ± 6.4</td>
<td>5.8 ± 3.0</td>
</tr>
<tr>
<td>Recovery</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RQ (%)</td>
<td>0.83 ± 0.05</td>
<td>0.82 ± 0.07</td>
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</tr>
<tr>
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<td>44.0 ± 15.1</td>
</tr>
<tr>
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<td>21.0 ± 9.5</td>
</tr>
</tbody>
</table>

*Significantly different from recovery: \( P < 0.04 \), \( P < 0.03 \), \( P < 0.01 \).
**Significantly different from exercise and recovery, \( P < 0.03 \).
***Significantly different from rest and recovery: \( P < 0.04 \), \( P < 0.01 \), \( P < 0.001 \).

### Table 4
Ventilatory indexes in the 3 groups during rest, exercise, and recovery

<table>
<thead>
<tr>
<th>Variable</th>
<th>CF group (n = 10)</th>
<th>CFDM group (n = 7)</th>
<th>Control group (n = 10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rest</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VE (L/min)</td>
<td>8.5 ± 1.6</td>
<td>8.5 ± 1.5</td>
<td>6.4 ± 1.1</td>
</tr>
<tr>
<td>VE (mL)</td>
<td>480.0 ± 116.8</td>
<td>464.0 ± 111.3</td>
<td>431.0 ± 142.8</td>
</tr>
<tr>
<td>RR (breaths/min)</td>
<td>18.6 ± 5.1</td>
<td>18.8 ± 3.7</td>
<td>15.7 ± 3.6</td>
</tr>
<tr>
<td>VO2 (mL · kg⁻¹ · min⁻¹)</td>
<td>3.8 ± 0.61</td>
<td>3.9 ± 0.73</td>
<td>3.5 ± 0.37</td>
</tr>
<tr>
<td>Exercise</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VE (L/min)</td>
<td>23.3 ± 4.9</td>
<td>23.7 ± 4.1</td>
<td>18.2 ± 3.0</td>
</tr>
<tr>
<td>VE (mL)</td>
<td>819.4 ± 197.4</td>
<td>840.4 ± 138.3</td>
<td>762.1 ± 205.8</td>
</tr>
<tr>
<td>RR (breaths/min)</td>
<td>29.5 ± 9.0</td>
<td>28.5 ± 5.1</td>
<td>25.1 ± 6.2</td>
</tr>
<tr>
<td>VO2 (mL · kg⁻¹ · min⁻¹)</td>
<td>12.6 ± 2.5</td>
<td>12.7 ± 1.6</td>
<td>12.5 ± 2.6</td>
</tr>
<tr>
<td>Recovery</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VE (L/min)</td>
<td>8.8 ± 2.0</td>
<td>9.4 ± 1.2</td>
<td>6.0 ± 1.3</td>
</tr>
<tr>
<td>VE (mL)</td>
<td>472.4 ± 119.1</td>
<td>498.7 ± 100.6</td>
<td>360.6 ± 88.9</td>
</tr>
<tr>
<td>RR (breaths/min)</td>
<td>19.5 ± 4.8</td>
<td>19.3 ± 3.6</td>
<td>16.9 ± 2.8</td>
</tr>
<tr>
<td>VO2 (mL · kg⁻¹ · min⁻¹)</td>
<td>4.1 ± 0.56</td>
<td>4.5 ± 0.78</td>
<td>3.2 ± 0.43</td>
</tr>
</tbody>
</table>

\( \pm \) SD. Normal values based on clinical standards are as follows: VE, 6.0–7.5 L/min; VE, 500 mL; RR, 12–15 breaths/min. VE, minute ventilation; VE, tidal volume; RR, respiratory rate; VO2, oxygen consumption; CF, cystic fibrosis; CFDM, CF plus diabetes mellitus.

*Significantly different from the CF and CFDM groups, \( P < 0.01 \) (post hoc Tukey-Kramer’s test).
**Significantly different from the control group, \( P < 0.02 \) (post hoc Tukey-Kramer’s test).
higher than that of the CF group. Increased glucagon secretions have been reported in type 1 and type 2 diabetic patients (3) and in patients with severe diabetic ketoacidosis (30). In patients with CFDM, glucagon concentrations have been described as normal or reduced (3, 30). Both hypoglucaemia and hyperglucagonemia have been reported in other studies (31). Kien et al (32) found elevated hepatic glucose production in children with CF. The CFDM group in our study had a higher glucagon concentration than the CF and control groups during rest (P < 0.05), exercise (NS), and recovery (NS). The blood glucagon concentration in the CFDM group was possibly higher during rest to guard against hypoglycaemia because neither decreased plasma insulin concentrations nor increased fat oxidation were observed after the overnight fast. The latter condition indicates a low blood glucose concentration or a shift in substrate utilization, which would stimulate the release of glucagon. However, because of the large number of variables measured in the blood profile and the small sample size, conclusions based on glucagon data must be made with caution.

The CFDM group tended to have a higher epinephrine concentration than the other 2 groups at the end of each study period. In addition, epinephrine concentrations in the CF and CFDM groups remained higher than baseline values at the end of the recovery period, whereas the control group had an epinephrine concentration that was lower than baseline at this time point. Despite these trends, no significant differences were found in epinephrine concentrations between the 3 groups and there was great variability in the catecholamine data. Catecholamines may serve as indicators of stress and are known to increase the basal metabolic rate by 7–15%, increase glucagon, decrease insulin production, increase glucose production by the liver (gluconeogenesis), increase glycogenolysis, and increase lipolysis. In addition, chronically elevated epinephrine concentrations result in hypoglycaemia and fat store depletion. In this study, we were unable to conclude that circulating catecholamines in the CFDM group contributed to the increased EE found during recovery. In one study, adult patients with CF (without DM) were found to have significantly higher epinephrine concentrations than control subjects (33). We hypothesized that chronically elevated epinephrine concentrations in patients with CF and CFDM may result in increased EE, hypoglycaemia, increased fat store depletion, and poor nutritional status. We believe these observed trends in epinephrine need further study.

This study was not designed specifically with the power to detect group differences in any particular index; thus, inferences about nonsignificant comparisons are particularly susceptible to type II errors. For instance, mean within-group EEs at rest and during exercise were not significantly different in the present study; however, these results were subject to type II error and thus should be interpreted with caution. On the other hand, these same comparisons may indicate trends that should be investigated in larger-scale studies not susceptible to type II error.

In this study, patients with CF and CFDM were able to maintain EE values within the normal range of the control group during rest and exercise periods, despite a significantly higher Ve. However, during recovery from exercise, the CF and CFDM groups used more energy than the control group and not only maintained a higher Ve, but a higher VO2 as well. Our data suggest that the elevated EE in both the CF and CFDM patients, during periods of recovery from mild exercise or activity, was due to increased breathing resulting from higher ventilatory require-

ments to compensate for a ventilation-to-perfusion mismatch. This additional energy requirement should be considered by CF and CFDM patients who choose to exercise regularly and should be incorporated into nutritional counseling goals intended for these patients. Some patients express concern about weight loss from exercise. Accurate assessments of energy use patterns in CF patients, which may differ from those in persons without CF, will allow patients to exercise comfortably, receive health benefits associated with regular exercise, and adjust their daily energy intake to compensate for the additional energy requirement during exercise recovery. Further studies of the energy requirements of patients with CF or CFDM during recovery periods postexercise, with larger sample sizes and more in-depth blood analyses (eg, of fatty acids, glycerol, lactate, glucagon, and epinephrine concentrations), are needed to advance the understanding of EE in these patients.

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REFERENCES

33. Elborn J, Cordon S, Western P, McDonald J, Shale D. Tumour necrosis factor alpha, resting energy expenditure and cachexia