Effect of Reduced Body Weight on Muscle Aerobic Capacity in Patients With COPD*

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Background: Reduced muscle aerobic capacity in COPD patients has been demonstrated in several laboratories by phosphorus magnetic resonance spectroscopy and by analysis of oxygen uptake (Vo2) kinetics. COPD patients are usually elderly, hypoxemic, poorly active with muscle atrophy, and often malnourished. Under these conditions there is usually reduction of O2 delivery to the tissues (bulk O2 flow), redistribution of fiber type within the muscle, capillary rarefaction, and decreased mitochondrial function, alterations all capable of reducing muscle aerobic capacity. In COPD, the effect of reduced body mass on muscle aerobic capacity has not been investigated (to our knowledge).

Methods: We studied 24 patients with stable COPD with moderate-to-severe airway obstruction (68±5 [SD] years; FEV1, 39±12% predicted; PaO2, 66±8 mm Hg; PaCO2, 41±3 mm Hg) with poor to normal nutritional status, as indicated by a low-normal percent of ideal body weight (IBW). Each subject first underwent 1-min maximal incremental cycle ergometer exercise for determination of Vo2 peak and lactate threshold (LT). Subsequently, they performed a 10-min moderate (80% of LT-Vo2) constant load exercise for determination of oxygen deficit (O2 DEF) and mean response time Vo2 (MRT). Vo2, CO2 output (VCO2), and minute ventilation were measured breath by breath.

Results: Patients displayed low Vo2 peak (1,094±47 [SE] mL/min), LT-Vo2 (35±3% predicted Vo2 max), and higher MRT-Vo2 (67±4 s). Univariate regression analysis showed that percent of IBW correlated with indexes of maximal and submaximal aerobic capacity; vs Vo2 peak, R=0.53 (p<0.01); vs MRT R=−0.77 (p<0.001). Using stepwise regression analysis, MRT correlated (R2=−0.70) with percent of IBW (p<0.01) and with PaO2 (p<0.05).

Conclusions: Reduced body mass has an independent negative effect on muscle aerobic capacity in COPD patients: this effect may explain the variability in exercise tolerance among patients with comparable ventilatory limitation.

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Key words: COPD; exercise; nutritional status; Vo2 kinetics

Abbreviations: ATP=adenosine triphosphate; BMI=body mass index; BR=breathing reserve; HR=heart rate; IBW=ideal body weight; MRT=mean response time; O2 DEF=oxygen deficit; FCr=phosphocreatine; ss=steady state; t½=half-times; TSF=triceps skinfold thickness; V/A=ventilation/perfusion; VCO2=CO2 production; VE=minute ventilation; Vo2=oxygen uptake

Recent studies have demonstrated that muscle aerobic capacity of stable hypoxemic COPD patients is impaired. Slow O2 uptake (Vo2) kinetics and large O2 deficit (O2 DEF) at submaximal workloads have been reported: inadequately cardiovascular adaptations and reduced ability of the peripheral muscles to generate energy via aerobic pathways were postulated as the underlying mechanisms. Phosphorus magnetic resonance spectroscopy studies...
have shown that these patients rely heavily on nonaerobic sources to sustain even light efforts; in addition, early occurrence of metabolic acidosis has been demonstrated in patients with mild-to-severe COPD exercising at moderate intensity.\textsuperscript{6,8} Oxygen supplementation has been shown to partially improve the derangements mentioned above.\textsuperscript{2,3} The recent report\textsuperscript{9,10} that physical training, by increasing muscle aerobic capacity, tends to normalize the \( \text{Vo}_2 \) kinetic curve lends support to the view of reliance on nonaerobic pathways for adenosine triphosphate (ATP) production.

A close relationship between poor muscle condition, reflected by reduction in percent of ideal body weight (IBW), and maximal aerobic capacity (\( \text{Vo}_2 \) peak) has been observed in several laboratories.\textsuperscript{11-13} The significance of this finding is unclear because factors other than malnutrition, particularly ventilatory limitation at maximal exercise level, might have affected \( \text{Vo}_2 \) peak. The submaximal approach, in which ventilatory limitation is no longer a confounding factor, should supply more precise information regarding a causal connection between poor nutritional state and aerobic capacity.

Analysis of \( \text{Vo}_2 \) kinetics during exercise provides a better understanding of the muscle oxidative machinery in health and in disease states.\textsuperscript{14} In healthy subjects, during the transition phases of moderate (ie, below lactate threshold) constant load exercise, \( \text{Vo}_2 \) increases toward steady-state value in an approximately exponential manner with half-times (\( t_{1/2} \)) of about 30 s, and reaches steady-state about 3 min after exercise onset: the shape of the \( \text{Vo}_2 \) curve reflects the ability of the exercising muscles to utilize \( \text{O}_2 \) from tissue stores and \( \text{O}_2 \) transported by the circulation\textsuperscript{15} as well as the energy level generated by phosphocreatine (PCR) breakdown and by anaerobic glycolysis until steady-state \( \text{Vo}_2 \) is reached.\textsuperscript{16-18}

The aim of the present study was to investigate the effect of reduced body weight on muscle aerobic capacity of COPD patients by correlating percent of IBW and muscle aerobic capacity expressed by the \( \text{Vo}_2 \) time constant. Multivariate regression analysis was utilized to assess the relative contribution of pertinent variables other than percent of IBW, such as age and degree of arterial hypoxemia, to the limited muscle aerobic capacity.

**Materials and Methods**

We studied 24 male COPD ambulatory patients with mild-to-severe stable airway obstruction and mild hypoxemia. Admission criteria included the following: clinical evidence of COPD, exertional dyspnea, FEV\textsubscript{1} \( \leq \)50% of predicted, room air PaO\textsubscript{2} \( \geq \)55\( \leq \)75 mm Hg, and body weight \( \leq \)120% of predicted ideal level. The pertinent clinical and functional characteristics of the subjects are summarized in Table 1. At the time of the study, patients had no sacral or ankle edema and no evidence of cor pulmonale or metabolic, renal, hepatic, or neuromuscular disorders. None of them had received systemic steroid therapy for at least 3 months. A stable regimen of bronchodilators with oral theophylline, inhaled \( \beta \)-stimulant, and inhaled steroids was maintained. The experimental protocol was approved by the Committee for Protection of Human Subjects, University of Rome, according to the declaration of Helsinki: all subjects signed an informed consent prior to initiation of the study.

**Nutritional Assessment**

On arrival at the laboratory at 8 AM after a light breakfast, weight and height were measured after the bladder was emptied and all clothes except for underwear were removed. As in most studies dealing with COPD patients, nutritional status was assessed through the calculation of the percent of IBW.\textsuperscript{19} For percent of IBW, the measured body weight was related to IBW calculated from the regression equation of weight/height for the midpoint of the weight range for a given height (from a minimal value for a small frame size to a maximal value for a large frame), from the Metropolitan Insurance tables.\textsuperscript{20} To allow comparisons with other studies, body mass index (BMI, kg/m\textsuperscript{2}=body weight/square of the height), an index independent of sex, height, and body frame, was also calculated. Triceps skinfold thickness (TSF), determined by Harpenden skinfold caliper (British Indicators Ltd; St. Albans, UK), was used to estimate body fat stores.\textsuperscript{19,21}

**Equipment**

Spirometry and arterial blood gas values were obtained before each bout of exercise to confirm clinical stability. Subjects exercised on an electromagnetically braked cycle ergometer (ERG-551; Bosch; Bisingen, Germany). Pulmonary gas exchange variables were determined breath by breath (P.K. Morgan Ltd; Kent, UK) as described below. Patients breathed through a mouthpiece; inspiratory and expiratory volumes were measured by a pneumotachometer (total dead space was 50 mL). Gas was drawn from the distal part of the pneumotachometer and concentrations of \( \text{O}_2 \) and \( \text{CO}_2 \) were determined by rapid response analyzer (\( \text{O}_2 \) zirconium, \( \text{CO}_2 \) infrared; P.K. Morgan Ltd). Before each test, a two-point calibration of the gas analyzers was performed using room air and a gas mixture from a tank of standard gas. ECG was monitored continuously at \( V_6 \) by means of a cardio scope; heart rate (HR) was derived from R-R intervals, and arterial \( \text{O}_2 \) saturation was watched continuously by pulse oximetry (Biox 3740; Ohmeda; Liberty Corner, NJ). \( \text{Vo}_2 \) (STPD), \( \text{CO}_2 \) production (V\( \text{CO}_2 \), STPD), minute ventilation (VE, BTPS), and end-tidal \( \text{CO}_2 \) were measured for each breath with the use of

<table>
<thead>
<tr>
<th>Table 1—Subjects’ Pertinent Characteristics</th>
<th>COPD Patients (n=24)</th>
<th>Control Subjects (n=10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>68±5 (59-76)</td>
<td>68±4 (62-75)</td>
</tr>
<tr>
<td>FEV\textsubscript{1}, % predicted</td>
<td>39±12\textsuperscript{3} (24-50)</td>
<td>96±2 (93-103)</td>
</tr>
<tr>
<td>FVC, % predicted</td>
<td>70±11\textsuperscript{11} (52-79)</td>
<td>97±5 (95-108)</td>
</tr>
<tr>
<td>PaO\textsubscript{2}, mm Hg</td>
<td>66±5 (55-75)</td>
<td>—</td>
</tr>
<tr>
<td>PaCO\textsubscript{2}, mm Hg</td>
<td>41±3 (38-48)</td>
<td>—</td>
</tr>
<tr>
<td>pH</td>
<td>7.41±0.03 (7.37-7.47)</td>
<td>—</td>
</tr>
<tr>
<td>% IBW</td>
<td>103±14 (76-120)</td>
<td>107±7 (98-118)</td>
</tr>
<tr>
<td>BMI, kg/m\textsuperscript{2}</td>
<td>25±4 (18-29)</td>
<td>25±2 (23-27)</td>
</tr>
<tr>
<td>TSF, mm</td>
<td>13±6 (4-25)</td>
<td>15±5 (10-25)</td>
</tr>
</tbody>
</table>

*p=0.001.

\( \text{Mean±SD. Range in parentheses.} \)
Maximal Exercise Test

Subjects underwent a 1-min incremental exercise test: after 3 min of rest and 3 min of unloaded pedaling, workload was increased until exhaustion, i.e., the point when they could no longer maintain the pedaling frequency of 50 rpm. The rate of workload increment was chosen on the basis of FEV\textsubscript{1} values: FEV\textsubscript{1}≤1 L; 5 W; FEV\textsubscript{1}>1≤1.5 L, 10 W; FEV\textsubscript{1}>1.5 L, 15 W. The lactate threshold (LT-Vo\textsubscript{2}) was determined from a plot of V\textsubscript{CO\textsubscript{2}} vs Vo\textsubscript{2} (modified “V-slope method”);\textsuperscript{23} the values were expressed as percent of predicted Vo\textsubscript{2} max.\textsuperscript{24} Other variables were obtained as follows: breathing rate (BR)=1-V\textsubscript{E} max/FEV\textsubscript{1}×40; O\textsubscript{2} pulse=Vo\textsubscript{2}/HR.

Moderate Constant Load Exercise

After 45 h from the incremental test, subjects performed an additional test consisting of a rest period of 5 min followed by 2 min of unloaded pedaling ("0") and then 10 min of cycling at a work rate approximately 80% of LT-Vo\textsubscript{2} determined during the maximal test. The three patients in whom LT-Vo\textsubscript{2} was not clearly discernible were exercised at 50% of the maximum workload achieved on the incremental test. The average values obtained during the last minute of unloaded pedaling ("0") was used as baseline; the average values obtained during the last 2 min of exercise were used as steady-state ("ss") data. O\textsubscript{2} DEF was calculated as the sum of the differences between the Vo\textsubscript{2} values measured at each minute before an ss was reached and the mean ss value. Mean response time (MRT), the time required to attain 60% of the ss Vo\textsubscript{2} value, was calculated according to the following formula:

\[ \text{MRT, s} = \left( \frac{\text{O}_2 \text{DEF/Vo}_2, \text{ss} - \text{Vo}_2, \text{ss}}{\text{Vo}_2, \text{ss}} \right) \times 60 \]

To further describe the speed of gas exchange kinetics, Vo\textsubscript{2}, V\textsubscript{CO\textsubscript{2}}, and Ve data from "0" to "ss" were fitted by a least squares gradient algorithm to a first-order monoeponential model; the individual t/2 values were subsequently computed and averaged to give the mean group values. The t/2 HR and t/2 O\textsubscript{2} pulse were also calculated.

Statistical Analyses

Group data are presented as mean values±SD or SE of mean where appropriate. Differences among measured parameters were determined by unpaired t test. Pearson’s product-moment correlation coefficient (R) analysis was used to detect correlations between criterion variables. Multiple regression analysis was performed to determine the best predictor of MRT from selected independent variables (age, percent of IBW, FEV\textsubscript{1}, and PaO\textsubscript{2}); the determination coefficient (R\textsuperscript{2}) was used to describe the goodness of fit equation to the experimental data. The level of statistical significance was set at p<0.05.

RESULTS

Table 1 shows that COPD patients had moderate-to-severe degree of airway obstruction, hypoxemia and, in most instances, normocapnia. Although mean percent of IBW, BMI, and T5F did not differ from those of control subjects, in the COPD group, a wider range of values was observed. Five of 24 COPD patients desaturated during exercise (ΔSatO\textsubscript{2}>4%) during the incremental test, but none of them desaturated during the constant load test.

Data obtained at peak exercise are shown in Table 2. Compared with control subjects, COPD patients displayed reductions in Vo\textsubscript{2} peak (1,094±47 vs 2,300±80 mL/min; p<0.001), LT-Vo\textsubscript{2} (35±3 vs 45±2%; p<0.05), and BR (14±4 vs 39±1%; p<0.001).

Compared with control subjects, during moderate exercise (Table 3), COPD patients, despite the lower Vo\textsubscript{2} ss, showed increased MRT (67±4 vs 42±1 s; p<0.01) and t/2 Ve\textsuperscript{O2} (51±4 vs 33±1 s; p<0.05) values confirming the slowing of Vo\textsubscript{2} kinetics in COPD patients compared with control subjects. t/2 V\textsubscript{CO\textsubscript{2}} and t/2 Ve\textsuperscript{O2} were also higher than those for control subjects, while t/2 HR and t/2 O\textsubscript{2} pulse were not different. The typical pattern of Vo\textsubscript{2} kinetics from "0" to ss, during the constant load test, in a COPD patient and in a control subject are shown in Figure 1.

### Table 2—Peak Exercise Data

<table>
<thead>
<tr>
<th></th>
<th>COPD Patients (n=24)</th>
<th>Control Subjects (n=10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>W max</td>
<td>65±3\textsuperscript{f}</td>
<td>132±1</td>
</tr>
<tr>
<td>Vo\textsubscript{2} peak, mL/min</td>
<td>1,094±47\textsuperscript{f}</td>
<td>2,300±80</td>
</tr>
<tr>
<td>LT, % predicted Vo\textsubscript{2} max</td>
<td>35±3\textsuperscript{f} (n=21)</td>
<td>45±2</td>
</tr>
<tr>
<td>BR, %</td>
<td>14±4\textsuperscript{f}</td>
<td>39±1</td>
</tr>
<tr>
<td>HR max, beats/min</td>
<td>116±2\textsuperscript{f}</td>
<td>150±3</td>
</tr>
<tr>
<td>O\textsubscript{2} pulse max</td>
<td>9.7±0.5\textsuperscript{f}</td>
<td>14.4±0.4</td>
</tr>
</tbody>
</table>

\textsuperscript{*}Mean±SE.  
\textsuperscript{p}<0.001.  
\textsuperscript{p}<0.05.

### Table 3—Gas Exchange Kinetics During Moderate Exercise

<table>
<thead>
<tr>
<th></th>
<th>COPD Patients (n=24)</th>
<th>Control Subjects (n=10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Watt ss</td>
<td>29±1</td>
<td>63±2</td>
</tr>
<tr>
<td>Vo\textsubscript{2} ss, mL/min</td>
<td>799±20\textsuperscript{f}</td>
<td>1,057±10</td>
</tr>
<tr>
<td>MRT, s</td>
<td>67±4\textsuperscript{f}</td>
<td>42±1</td>
</tr>
<tr>
<td>t/2 Ve\textsuperscript{O2}, s</td>
<td>51±4\textsuperscript{f}</td>
<td>33±1</td>
</tr>
<tr>
<td>V\textsubscript{CO\textsubscript{2}} ss, mL/min</td>
<td>727±33\textsuperscript{f}</td>
<td>919±15</td>
</tr>
<tr>
<td>t/2 Ve\textsuperscript{O2}, s</td>
<td>68±6\textsuperscript{f}</td>
<td>43±1</td>
</tr>
<tr>
<td>t/2 Ve, s</td>
<td>74±6\textsuperscript{f}</td>
<td>45±1</td>
</tr>
<tr>
<td>t/2 HR, s</td>
<td>40±6</td>
<td>39±1</td>
</tr>
<tr>
<td>t/2 O\textsubscript{2} pulse, s</td>
<td>37±3</td>
<td>41±1</td>
</tr>
</tbody>
</table>

\textsuperscript{*}Mean±SE.  
\textsuperscript{p}<0.001.  
\textsuperscript{p}<0.05.
Table 4 is a correlation matrix for the variables included in the analyses. Figure 2 shows that the decrement in nutritional state paralleled the reduction in muscle aerobic capacity, as indicated by the significant negative correlation between MRT and percent of IBW ($R=-0.77$; $p<0.001$). Results were the same when BMI was used instead of percent of IBW or $t_{1/2}$Vo$_2$ instead of MRT. $t_{1/2}$Vo$_2$ correlated less well with percent of IBW ($R=-0.46$, $p<0.05$) than MRT; $t_{1/2}$Ve did not correlate with percent of IBW.

In the stepwise regression test, MRTs were introduced as dependent variables, and age, FEV$_1$ percent of IBW, and PaO$_2$ were introduced as independent variables; MRT correlated ($R^2=-0.70$) with percent of IBW ($p<0.01$) and with PaO$_2$ ($p=0.05$).

In control subjects, nutritional status (percent of IBW or BMI) did not correlate with variables measured during exercise.

**Table 4—Matrix of Correlation Coefficients in COPD**

<table>
<thead>
<tr>
<th>Variables</th>
<th>IBW % predicted</th>
<th>Vo$_2$ peak</th>
<th>LT*</th>
<th>MRT</th>
<th>FEV$_1$</th>
<th>PaO$_2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>IBW, % predicted</td>
<td>1.00</td>
<td>0.53</td>
<td>0.83</td>
<td>-0.77</td>
<td>0.20</td>
<td>0.74</td>
</tr>
<tr>
<td>Vo$_2$ peak, mL/min</td>
<td>1.00</td>
<td>0.74</td>
<td>-0.51</td>
<td>0.18</td>
<td>0.32</td>
<td></td>
</tr>
<tr>
<td>LT, % predicted Vo$_2$</td>
<td>1.00</td>
<td>-0.70</td>
<td>0.27</td>
<td>0.67</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MRT, s</td>
<td>1.00</td>
<td>-0.24</td>
<td>-0.63</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FEV$_1$, % predicted</td>
<td>1.00</td>
<td>0.41</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PaO$_2$, mm Hg</td>
<td>1.00</td>
<td></td>
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</table>

*$n=24$.

**DISCUSSION**

The most salient finding of our study is the inverse correlation between percent of IBW and Vo$_2$ time constant (MRT) during moderate exercise (Fig. 2), demonstrating that in COPD patients, the decline in body mass parallels the impairment of muscle aerobic capacity. The energy requirements of these patients must therefore be fulfilled via nonaerobic pathways, namely PCR breakdown and/or anaerobic glycolysis, even for light physical efforts. Additional observations during the maximal and the submaximal tests confirming the poor aerobic capacity of our patients were the decrease in Vo$_2$ peak, the reduction in LT, and the slowing of Vo$_2$ kinetics. Each of these three abnormalities could be correlated with percent of IBW. In contrast, the correlations of FEV$_1$ with these three variables was of borderline significance. Taken together, the above findings strongly suggest that in COPD patients, factors other than ventilatory limitation, such as altered peripheral blood flow and/or poor muscle energetics, play a major role in hindering exercise aerobic capacity. This is certainly true for moderate workloads where, in contrast to high levels of exercise, ventilation is not a limiting factor. The recent report that physical training can return Vo$_2$ time constants toward normal levels by increasing muscle aerobic capacity lends support to this view.\(^9,10\)

Although we found a close correlation between indirect indexes of muscle aerobic metabolism and nutritional status, this does not necessarily mean that relationships are causal; also, we cannot exclude that
malnutrition influenced gas exchange kinetics independently from COPD. However, we can speculate on possible mechanisms for the observed findings. Modern views hold that in normal subjects, VO₂ kinetics, and therefore muscle aerobic capacity, are determined by the rate of oxygen delivery (bulk O₂ flow) to the exercising muscle or by “inertia” of the intramuscular oxidative machinery caused by rate-limiting step(s) along the pathways of aerobic glycolysis, β-oxidation of fats, tricarboxylic acid cycle, and mitochondrial respiratory chain. The possible role of maldistribution of blood flow to fibers with high oxygen requirement cannot be explored with methods available today. Recently, Grassi and coworkers have demonstrated that bulk O₂ delivery to the working muscle does not limit VO₂ kinetics, at least in normal individuals.

Nery et al. were the first to report that in patients with mild COPD and slight hypoxemia exercising at moderate workloads, VO₂ kinetics are slow. The authors attributed this finding to inadequate hemodynamic adaptations. Recently, on the basis of previous observations in normal subjects, Wasserman and coworkers have postulated that the slow VO₂ kinetics observed by Nery et al. were due to an increased rate of anaerobic glycolysis with lactate formation. Even though the level at which patients exercised was chosen to be below the LT-VO₂, some contribution from increased lactic acid production cannot be entirely excluded; in our study, the following speaks against this view. (1) In all the patients in whom LT could be detected by the V-slope method, the work rates selected were at least 10 W below the observed LT-VO₂ values. The remaining three patients, in whom the LT was not clearly discernible, precautionally were exercised at 50% of maximal workload achieved on the incremental test. (2) In all subjects, VCO₂ ss never exceeded VO₂ ss. (3) During the constant load test, VO₂ reached the ss condition in all tests.

Palange et al., in addition to confirming the observations of Nery et al., demonstrated that short-term 30% O₂ supplementation tends to normalize O₂ Dff and VO₂ kinetics without affecting other physiologic variables. This finding lends further support to the view that peripheral muscle dysfunction is the primary cause of altered gas exchange kinetics in COPD patients. None of the previous studies on VO₂ kinetics in exercising COPD patients has tested the hypothesis that reduction in body weight acts as an independent variable in impairing muscle aerobic capacity, and thus, in limiting exercise tolerance.

The mechanisms responsible for the reduced aerobic capacity in COPD patients are unknown. We postulate that they are, in type, the same as those proposed for normal elderly individuals but greater in magnitude. COPD patients are usually elderly, poorly active (with variable degree of muscle atrophy), hypoxic, and often malnourished. Within the muscle, such factors, individually or more likely in some combination, lead to alterations in fiber type distribution, reduction in capillary density, decrease in mitochondrial population, and “inertia” within the oxidative machinery. A reduction in bulk O₂ delivery to the exercising muscles due to poor hemodynamic adaptations and/or reduced O₂ content, with attendant greater dependency on PCR as metabolic fuel, might have been operative in our patients. The relatively normal t½ HR and t½ O₂ pulse mitigate against this hypothesis (although we cannot assure that the response amplitude was appropriate to the metabolic demand). Therefore, inertia of the oxidative enzyme system in the exercising muscle, perhaps in combination with inadequate flow to fibers with high O₂ requirements, appears to be the most likely cause of the findings observed. At this time, and to our knowledge, there is no method for proving this hypothesis.

Our results are in keeping with previous reports in which different methodologic approaches were utilized. Recent observations made with the use of 31P magnetic resonance spectroscopy suggest that the oxidative metabolism of skeletal muscle in COPD patients is significantly altered. Using biopsy techniques, it has been shown that peripheral and respiratory muscles of COPD patients are deficient in PCR and ATP. Previous studies have demonstrated a negative influence of the reduction in lean body mass and muscle strength on exercise performance in COPD patients. Recently, Maltais and coworkers have indicated that in COPD patients, excessive lactate production during exercise and reduced oxidative capacity of skeletal muscle are interrelated. Only sparse data exist in the literature correlating nutritional state with peripheral muscle energetics: the review article by Wilson et al. suggests that “malnutrition may affect muscle function but the significance of this effect in patients with COPD requires further investigation.” In the present study, we observed a close correlation between degree of malnutrition and slowing of gas exchange kinetics; however, we cannot exclude that reduction in body mass negatively influenced VO₂ kinetics independently from COPD. A patient’s nutritional state was assessed by measuring percent of IBW and BMI; although these indexes may not entirely reflect lean body mass, they are easily obtainable and have been widely used in relating weight to health, in normal and pathologic states.

Two groups of investigators have reported that in malnourished patients with stable, advanced COPD, the degree of weight loss bears no relation to
the work capacity at submaximal levels. In both instances, the physiologic end point was the distance covered during a fixed time period (6- and 12-min walking test). Recently, we compared the adaptations to walking and cycling in a group of COPD patients.34 Our results showed that in COPD patients, the ability of walking is primarily limited by an increase in ventilatory demand possibly related to neurogenic reflexes from arm movements; by contrast, during cycling, the arms are supported and chest movements are more coordinated. In the present work, we studied a group of similar patients during submaximal exercise of comparable intensity but utilizing a different experimental design. We monitored VO₂ kinetics and related parameters during short bouts of cycloergometer exercise, a method more sensitive in disclosing correlations between weight loss and muscle work capacity. To define more precisely the intrinsic rate of the oxidative machinery, we analyzed VO₂ kinetics during the transition from the light prior exercise (unloaded pedaling): with this protocol, the contribution of phase I hemodynamic adaptations (which may be quite variable) and the contribution of O₂ stores (again variable in size) to the size of the O₂ DEF are largely eliminated and markedly reduced, respectively;35 the only remaining operative mechanism is the contribution of nonaerobic energy sources, mostly PCr breakdown.

The influence of ventilation/perfusion (VA/Q) inhomogeneity on gas exchange kinetics in COPD patients has not been studied extensively. VO₂ kinetics are expected to be faster in the low VA/Q lung units and slower in high VA/Q units. Poole and coworkers36 studied the work efficiency of exercising muscles in healthy subjects and reported a close correlation between lung VO₂ and leg VO₂; the authors inferred that in patients with obstructive pulmonary disease, the study of muscle energetics by pulmonary gas exchange may have potential limitations. The recent evidence of Griffiths and coworkers9 and Otsuka and coworkers10 of a speeding of VO₂ kinetics as the result of a training in COPD, in the absence of any significant change in lung function indexes, speaks in favor of the usefulness of the VO₂ kinetics approach in the evaluation of muscle aerobic capacity of COPD patients.

The ability to increase ventilation is reduced in COPD patients. The more advanced the disease, the more impaired the exercise tolerance should be. However, as pointed out by Bauerle and Yones,37 the reduction in FEV₁ is not a very good predictor of exercise intolerance. The studies in which this relationship was examined have indicated that only 30 to 60% of the variability in exercise tolerance among COPD patients can be accounted for by the reduction in FEV₁. Clearly, factors other than ventilatory limitation play an important role in reducing exercise capacity in COPD patients. To our knowledge, the influence of body mass on muscle aerobic capacity of COPD patients has not been investigated. In the present study, in addition to confirming our previous observation (positive correlation between maximal aerobic capacity, ie, VO₂ peak and percent of IBW), we documented a strong influence of body weight on indexes of muscle aerobic capacity at submaximal level of exercise. The reduction in aerobic capacity paralleled very closely the decrease in body weight and, less nearly, the reduction in PaO₂. FEV₁ was not predictive of either maximal (VO₂ peak) or submaximal (MRT) aerobic capacity. Percent of IBW correlated less well with t½ VO₂ (R = -0.46, p<0.05) than with MRT; this is likely due to the larger CO₂ tissue store capacitance compared with O₂.

In the past, the inability of most COPD patients to reach the LT was attributed almost entirely to ventilatory limitation. Recently, it has been shown that the development of lactic acidosis during the early phases of exercise in COPD is a common event.5-8,23 This phenomenon has been attributed to inadequate O₂ supply to the exercising peripheral muscles.6 Alternatively, muscle inactivity may lead to reduced intramuscular ATP turnover and decreased concentrations of PCr with an early switch toward anaerobic glycolysis.32 Whatever the underlying mechanisms, excessive lactate generation mandates a large increase in ventilatory demand with a further reduction in work capacity.8

Our findings, preliminary in nature, are significant because they propose a partial explanation for the beneficial effect of therapeutic interventions, in particular the restoration of peripheral muscle function with rehabilitation programs. More work remains to be done to validate this hypothesis.

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