ORIGINAL RESEARCH

Prior intense exercise reduces arterial carbon dioxide pressure in extreme obesity

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Abstract

Purpose: Unlike normal weight individuals, individuals with extreme obesity do not show a decrease in arterial carbon dioxide pressure (PaCO₂) from rest to peak exercise. This indicates that breathing is compromised. The objective of this study was to determine if prior high intensity exercise lowers PaCO₂ in comparison with a first bout, normalized for the same metabolic rate.

Methods: Oxygen consumption during incremental, ramped exercise was matched to constant workload exercise (75% of peak power). Both protocols were to volitional exhaustion 39 ± 8 min apart. Eleven obese subjects (BMI = 47 ± 8 kg/m², aerobic capacity = 2.3 ± 0.6 L/min) were evaluated. Forty paired samples were obtained at the same metabolic rate between the two protocols.

Results: The mean absolute difference and 95% CI were large for arterial oxygen pressure (PaO₂) = 9 (6, 11) mmHg and alveolar to arterial oxygen pressure difference (AaDO₂) = 7 (5, 8) mmHg. The mean absolute difference for arterial oxyhemoglobin saturation (%SaO₂) = 0.5 (0.4, 0.7) %; PaCO₂ = 4 (3, 4) mmHg; physiological dead space to tidal volume ratio (V_D/V_T) = 0.04 (0.03, 0.05); and alveolar ventilation (VA) = 3 (2, 4) L/min. The recovery period after the first bout of exercise reduced the PaCO₂ by 3 mmHg when matched for similar metabolic rates. Constant workload exercise predicted VA, %SaO₂, V_D/V_T, and PaCO₂, but

not PaO₂ or AaDO₂ during incremental exercise at similar metabolic rates.

Conclusion: Given a sufficient chemical stimulus, obese subjects will attempt to breathe more, although this does not mean more VA, which removes CO₂.

In normal-weight individuals (Body mass index or BMI = 18.5 to 24.9 kg/m²), arterial carbon dioxide pressure (PaCO₂) usually decreases from rest to peak exercise. The drop in PaCO₂ is about 5 to 6 mmHg (from a resting value of 38 - 40 mmHg to a peak exercise value of ≤ 34 mmHg).¹⁻³ In contrast, evidence suggests that subjects with extreme obesity (BMI ≥ 40 kg/m²) maintain PaCO₂ from rest to peak exercise.^{4,5} A PaCO₂ ≥ 35.0 mmHg during strenuous exercise suggests poor compensatory exercise hyperventilation, and PaCO₂ ≥ 38.0 mmHg suggests absence of a complete hyperventilatory response.⁶ Of course, those definitions suggest that hyperventilation during exercise is only “compensatory” if it is necessary to prevent decreases in arterial oxygen pressure (PaO₂). If PaCO₂ does not decrease between rest and peak exer-

cise, there may still be some issues with breathing, as normal individuals do have a reduction in PaCO_2 of 5 to 6 mmHg between rest and maximal exertion.¹⁻³ About 75% of individuals with extreme obesity have a $\text{PaCO}_2 \geq 35.0$ mmHg at peak exercise despite arterial plasma lactate (a breathing stimulant) levels of 8.0 mmol/L.⁴ This demonstrates that most individuals with extreme obesity have a “poor breathing response” to strenuous, near maximal exercise that is likely mechanical in nature.

Weight loss has been shown to improve breathing in subjects with extreme obesity: a 21 kg weight loss reduced the PaCO_2 by 3 to 4 mmHg at peak exercise in comparison with PaCO_2 before weight loss.⁷ This improvement in breathing implies that weight loss reduces mechanical constraint around the chest wall, leading to increased alveolar ventilation at a given metabolic rate.

Another more immediate way to improve the ventilatory response to exercise in subjects with extreme obesity could be the use of repeat exercise. To date, no such study has addressed the use of repeat exercise to improve breathing in subjects with extreme obesity. There are data to show that PaCO_2 during the second bout of exercise in non-obese humans and horses is usually lower in the second bout in comparison with the first⁸⁻¹⁰ although other studies have report conflicting results,^{11,12} while mean arterial oxygen pressure (PaO_2) may increase in the second bout of exercise.⁹ If repeat exercise reduces PaCO_2 in subjects with extreme obesity, this reduction in PaCO_2 must be caused by something other than a reduction in mechanical constraint, as weight loss would not have occurred during one test session. If repeat exercise does not affect PaCO_2 then there must be a mechanical constraint to breathing. The objective of this study was to examine if and how a second bout of intense exercise affects arterial blood-gas status in subjects with extreme obesity. We hypothesized that PaCO_2 in extremely obese individuals would not change during a second exercise bout 40 minutes later because extremely obese individuals show a limited reduction in

PaCO_2 from rest to maximum exercise,^{4,5} which is mostly mechanical in nature.

Methods

Eleven extremely obese subjects participated in this study. Height and weight were assessed and lean and fat mass measured from an 8 polar bioelectrical impedance device¹³ to estimate excess weight.¹⁴ Some of these subjects were previously recruited from a much larger study⁴. Following IRB approval, all subjects signed an informed consent and arterial catheterization was performed. Initial (1) anthropometrics, (2) spirometry, (3) resting oxygen consumption and (4) arterial blood gases (ABG's) were measured. Incremental exercise testing commenced, with ABG sampling every minute. Following incremental exercise subjects rested for ~40 min and resting oxygen consumption and ABG's were again measured. Constant workload (CW) exercise commenced for ~5 min above ventilatory threshold (~75% of peak power output) and ABG's were sampled every minute.

Spirometry

Forced vital capacity (FVC), forced expiratory volume in one second (FEV_1), peak expiratory flow rate (PEF), and forced expiratory flow rate were measured over the middle half of expiration (FEF_{25-75}), with the Hyp'Air pulmonary function system (Dinant, Belgium). The predictive values were obtained from Hankinson *et al.*¹⁵

Maximal incremental protocol

Exercise testing was performed on an electrically-braked cycle ergometer (Velotron Dynafit Pro, Racermate Inc., Seattle, WA). The maximal incremental protocol commenced at 5 W and increased 1 W every 2 - 6 s (10 - 30 W/min) until volitional exhaustion in all subjects within 8 - 12 min. A facemask with an instrumental deadspace of 50 ml was used. Measured

$\dot{V}O_{2peak}$ was compared to the predicted $\dot{V}O_{2peak}$ for age, gender, and height.¹⁶ Cardiopulmonary variables including oxygen consumption ($\dot{V}O_2$), minute ventilation ($\dot{V}_E$), carbon dioxide production ($\dot{V}CO_2$), respiratory exchange ratio (RER) and the concentration of mixed expired CO₂ (%FECO₂) were assessed with a metabolic cart (model VMax 229LV, Sensorsmedics®, Yorba Linda, CA) using the breath-by-breath option. The three highest consecutive $\dot{V}O_2$ values (averaged over 20 s intervals) defined $\dot{V}O_{2peak}$. Therefore, the highest $\dot{V}O_2$ over a 60 s period defined $\dot{V}O_{2peak}$. Heart rate (HR) was recorded by 3-lead ECG (Cardiacap/5, Datex Ohmeda, Louisville, CO). Subject data were compared to predicted values for peak power output, peak O_{2pulse} , and $\dot{V}_{Epeak}$.¹⁶

Constant workload protocol

The peak power output from the maximal incremental protocol was used to determine the target power output for the constant workload protocol, given that fit individuals can exercise at ~80% peak power output for about five min.⁸ Extremely obese individuals were assumed to be able to exercise for the same time and near the same relative percentage of peak power output, so 75% of peak power output was chosen for constant workload protocol testing. This 75% of individual peak power output exceeded the ventilatory threshold, and $\dot{V}O_{2peak}$ was achieved within three min.

Arterial catheterization

Catheterization of either radial artery was performed before exercise testing,⁴ with peak blood temperature recorded during sampling by a rapid response thermocouple (IT-18, Physitemp, Clifton, NJ, USA). Five mL were withdrawn, initially, and then 2 mL samples were withdrawn at rest, every minute throughout exercise, and at peak exercise in both exercise protocols

for analysis of ABG's. Samples were stored on ice and analyzed within 10 min for PaO₂, PaCO₂, pH_a, and oxygen saturation (%SaO₂) with an ABL725 Analyzer (Radiometer, Copenhagen, Denmark). The ideal alveolar gas equation was used to calculate PAO₂ and the AaDO₂.¹⁷ The physiological dead space to tidal volume ratio (V_D/V_T) was calculated as $(PaCO_2 - PECO_2)/PaCO_2$ where PECO₂ is the partial pressure of mixed expired CO₂. Temperature-corrected PaO₂, PaCO₂ and pH values were based on section 4.3.2 in the guidelines of the Clinical Laboratory Standards Institute.¹⁸

Statistical analyses

Gas exchange responses for the two exercise protocols matched to the same $\dot{V}O_2$ were compared by linear regression, including alveolar ventilation ($\dot{V}_A$), AaDO₂, PaO₂, PaCO₂, V_D/V_T , and %SaO₂. A paired *t*-test was used to compare mean absolute differences for the following variables between the two exercise protocols matched to the same $\dot{V}O_2$: $\dot{V}_A$, tidal volume, respiratory rate, %SaO₂, PaO₂, PaCO₂, pH, AaDO₂, V_D/V_T , arterial plasma lactate concentration, and arterial plasma [K⁺]. Resting values and exercise values above the ventilatory threshold were separated and then a paired *t*-test was performed to compare the mean difference between the variables in both protocols matched for $\dot{V}O_2$. The ventilatory threshold was determined during the maximal incremental protocol from the V-slope method, which corresponds to the breakpoint in $\dot{V}CO_2$ as a function $\dot{V}O_2$ relationship.¹⁹

The mean absolute difference between the two protocols of each variable was calculated by removing all the negative values and replacing with positive values. The 95% confidence interval (95% CI) for accuracy between the two protocols was calculated as the mean absolute difference ± 1.96 multiplied by the standard error of the mean. The *t*-tests were performed using

SPSS version 15.0 (SPSS Inc. Chicago, IL), with statistical significance at $p < 0.05$.

Results

Eleven extremely obese subjects ($\text{BMI} = 47 \text{ kg/m}^2$, average excess weight of 71 kg) completed the study (Table 1). Their mean $\dot{V}O_{2\text{peak}}$ by the maximal incremental protocol was 17 mL/kg/min , below the 1st percentile for aerobic capacity by age and gender.²⁰ Their aerobic capacity was $106 \pm 15\%$ predicted as were their peak power output ($108 \pm 15\%$), HR ($97 \pm 4\%$), and $\dot{V}_E$ ($112 \pm 17\%$) at peak exercise.¹⁶ Peak O_2 pulse was significantly lower ($75 \pm 12\%$) than predicted.¹⁶

During exercise at 75% peak power output, which occurred $39 \pm 8 \text{ min}$ after maximal incremental protocol, $\dot{V}O_{2\text{peak}}$ was reached within 3 min, and subjects lasted a total of $4.6 \pm 0.7 \text{ min}$ (Table 2, Figure 1).

Forty paired ABG's (among 160 total samples) were obtained at the same $\dot{V}O_2$ during the two protocols, with a maximal difference in $\dot{V}O_2$ of 100 mL/min for any pair at rest ($n = 10$ paired samples) or during exercise ($n = 30$ paired samples). The mean difference in PaO_2 and AaDO_2 at rest between the two protocols was 3 and 2 mmHg, respectively, and for SaO_2 was 0.0%, ($p = \text{ns}$, Table 3). At exercise above the ventilatory threshold (constant workload protocol),

TABLE 1. Subject characteristics

n=11 (women = 8; men = 3)	Mean (SD)	Range
<i>Body Parameters</i>		
Age (years)	39 (9)	27 – 58
Height (cm)	168 (7)	158 – 181
Weight (kg)	134.8 (28.1)	93.5 – 181.0
Excess weight (kg)	71.4 (25.7)	35.4 – 113.4
Percent excess weight	200 (35)	160 – 264
Body mass index (kg/m^2)	47.4 (8.3)	36.5 – 61.9
Body surface area (m^2)	2.4 (0.3)	1.9 – 2.9
Waist circumference (cm)	134.0 (17.8)	95.0 – 157
Hip circumference (cm)	142.3 (20.6)	108.0 – 171.0
Waist to hip ratio	0.95 (0.08)	0.81 – 1.09
Fat Free mass (kg) (including muscle mass and bone mineral mass)	66.6 (11.9)	49.0 – 82.4
Fat mass (kg)	68.2 (18.5)	44.5 – 98.6
Body fat (%)	50.1 (4.7)	41.4 – 55.7
<i>Baseline Spirometry</i>		
FEV ₁ (L)	3.34 (0.62)	2.54 – 4.51
FVC (L)	4.22 (0.71)	3.17 – 5.32
FEV ₁ /FVC (%)	79 (5)	70 – 86
PEF (L/s)	7.48 (2.71)	4.19 – 13.34
FEF ₂₅₋₇₅ (L/s)	4.15 (1.25)	2.97 – 6.65
<i>Baseline Blood Parameters</i>		
Hemoglobin (g/L)	138 (12)	124 – 159
Hematocrit	0.402 (0.034)	0.340 – 0.457
Hb A1C	0.060 (0.014)	0.050 – 0.098

*Predicted value significantly different than measured value ($P < 0.05$). Body surface area (BSA) was calculated as $0.0097 \cdot (\text{height in cm} + \text{weight in kg}) - 0.545$. FEV₁ = forced expiratory volume in 1 second; FVC = forced vital capacity; PEF = peak expiratory flow; FEF₂₅₋₇₅ = forced expiratory flow over the middle half of expiration; The spirometry values are a percentage of normal values predicted for men and women of same height and age.¹⁵ Hb A1C = glycated Hb

TABLE 2. Cardiopulmonary parameters at peak exercise during the two different exercise tests

n=11 (women = 8; men = 3)	Mean (SD)	Range
<i>Incremental exercise (VO₂max test)</i>		
Cardiopulmonary parameters at peak exercise (average over the final minute)		
$\dot{V}O_2$ (mL/kg/min)	16.9 (3.3)	12.6 – 24.5
$\dot{V}O_2$ (L/min)	2.26 (0.57)	1.45 – 3.35
$\dot{V}O_2$ (mL/kgFFM/min)	33.8 (5.1)	26.9 – 43.6
Power output (W)	171 (38)	110 – 236
$\dot{V}_E$ (L/min) BTPS	84.8 (17.4)	64.2 – 112.8
RER	1.21 (0.07)	1.11 – 1.30
$\dot{V}CO_2$ (L/min)	2.72 (0.58)	2.46 – 3.72
HR (beats/min)	168 (7)	155 – 178
O ₂ pulse (mL/beat)	13.5 (3.8)	8.9 – 21.6
Arterial plasma lactate concentration (mmol/L)	8.5 (1.9)	5.8 – 12.0
Time to exhaustion (min)	8.4 (1.4)	6 – 9
<i>Constant Workload (75% of peak power output)</i>		
Cardiopulmonary parameters averaged over the final minute		
$\dot{V}O_2$ (mL/kg/min)	17.1 (3.1)	13.1 – 23.3
$\dot{V}O_2$ (L/min)	2.28 (0.47)	1.22 – 2.87
$\dot{V}O_2$ (mL/kgFFM/min)	34.3 (5.1)	25.0 – 41.5
Power output (W)	125 (26)	70 – 165
$\dot{V}_E$ (L/min) BTPS	88.5 (15.5)	60.3 – 109.5
RER	1.12 (0.05)	1.02 – 1.20
$\dot{V}CO_2$ (L/min)	2.55 (0.49)	1.40 – 3.16
HR (beats/min)	170 (11)	146–182
O ₂ pulse (mL/beat)	13.7 (3.2)	7.3 – 18.0
Arterial plasma lactate concentration (mmol/L)	10.8 (2.1)	7.0 – 13.7
Time to exhaustion (min)	4.6 (0.7)	3 – 5

* $\dot{V}O_2$ = oxygen consumption; $\dot{V}CO_2$ = carbon dioxide production; $\dot{V}_E$ = minute ventilation; RER = respiratory exchange ratio; HR = heart rate; O₂ pulse = oxygen pulse, or the ratio of oxygen consumption in ml/min divided by heart rate in beats/min.

PaO₂ was 4 mmHg lower, and AaDO₂ was 4 mmHg higher when matched for the same $\dot{V}O_2$ ($p < 0.05$).

The mean absolute difference was similar for both PaO₂ and AaDO₂ at rest and during exercise, so the resting and exercise differences were combined and reported in Table 4. Linear regressions comparing maximal incremental protocol and constant workload protocol matched by $\dot{V}O_2$ were significant for only

PaCO₂, %SaO₂, $\dot{V}A$, and V_D/V_T (Figure 4). The recovery period between the maximal incremental protocol and constant workload protocol protocols further reduced the PaCO₂ as the PaCO₂ at the start of exercise was already decreased by ~3 mmHg, even when matched for $\dot{V}O_2$ (Table 3, Figure 3C).

Discussion

The purpose of this study was to examine the effects of repeat exercise on PaCO_2 in subjects with extreme obesity. Results indicated that it was not the second bout of intense exercise *per se* that reduced the PaCO_2 but it was the recovery period following the first bout (maximal incremental protocol) that reduced the PaCO_2 . The PaCO_2 at rest was 3 mmHg lower at the beginning of the second bout of exercise compared with the first bout, and did not appreciably change with exercise suggesting that the recovery period was responsible for the reduction in PaCO_2 . These data support the hypothesis, as PaCO_2 did not change throughout the second bout of exercise; however, the PaCO_2 was lower through the recovery period and throughout the second bout of exercise (Figure 3C, Table 3).

We also found that the $\dot{V}_A$, % SaO_2 , $\dot{V}_D/\dot{V}_T$, and PaCO_2 , but not PaO_2 or AaDO_2 , from the constant workload protocol could predict maximal incremental protocol responses matched at a similar $\dot{V}\text{O}_2$.

The effects of prior exercise on PaCO_2

The effects of prior exercise on ABG's have been studied in humans^{8,9,11,12} to evaluate diffusion limitation as a mechanism of exercise-induced hypoxemia. Since this study uses two sequential exercise protocols, our study can be considered to have used prior exercise to examine ABG's. As shown by Zeballos and Weisman¹⁰ and the current study, prior intense exercise usually decreases PaCO_2 ⁹ resulting in a lower PaCO_2 in the second bout of exercise in comparison with the first;^{8,9} although this finding is not consistent.^{11,12} As well, PaO_2 may increase in the second bout of exercise.⁹ Since gas exchange does not decline, and may even improve during the second exercise bout, any pulmonary edema triggered by intense exercise²¹ would be too mild to affect diffusion.⁸ Thus, any exercise-induced hypoxemia probably arises from ventilation-perfusion mismatching and intrapulmonary shunting and not from interstitial

FIGURE 1. Oxygen consumption in both exercise protocols in extremely obese subjects. Filled circles = First bout of exercise, the incremental exercise protocol to volitional exhaustion; Open circles = Second bout of exercise, constant workload protocol, at 75% of peak power output (followed 40 minutes after the incremental exercise protocol). Mean $\pm$ SEM, $n = 11$ subjects.

edema.^{8,9} In this study, the second bout of exercise resulted in a lower PaO_2 and a higher AaDO_2 when matched for the same exercise $\dot{V}\text{O}_2$, suggesting that mild interstitial edema was present. If gas exchange is examined over minutes 4 and 5 of the constant workload protocol (Figure 2), PaO_2 and AaDO_2 are similar values for minutes 6 to 9 of the maximal incremental protocol. Therefore, repeat exercise did not clinically affect pulmonary gas exchange in these subjects. When matched for the same exercise $\dot{V}\text{O}_2$, 54% of the variance in the increase in arterial lactate in the second bout of exercise compared to that of the first bout was accounted for by the reduction in PaCO_2 in the second bout. When resting data were added to the exercise data for the two protocols, the variance decreases slightly, to 36% (change in $\text{PaCO}_2 = -0.694$, change in lactate concentration -2.106 , $r^2 = 0.36$, $\text{SEE} = 2.1$, $P < 0.001$, $F\text{-Ratio} = 21.5$). This suggests that the increase in arterial [lactate] from the first bout of exercise is strongly related to the drop in PaCO_2 during recovery. If there was a true mechanical con-

TABLE 3. Pulmonary gas exchange variables measured at the same $\dot{V}O_2$ during the maximal incremental protocol and constant workload protocol.

	Pooled (n = 10 paired samples per variable)		
<i>Rest</i>	<i>Incremental exercise protocol</i>	<i>Constant workload protocol</i>	p Value
$\dot{V}O_2$ (L/min)	0.36 (0.07)	0.38 (0.09)	0.15
$\dot{V}A$ (L/min)	5.2 (2.3)	5.0 (1.3)	0.75
$\dot{V}CO_2$ (L/min)	0.30 (0.07)	0.30 (0.07)	0.63
RER	0.83 (0.07)	0.79 (0.06)	< 0.01*
Tidal volume (L/breath)	0.8 (0.2)	0.8 (0.2)	0.20
Respiratory rate (breaths/min)	15.6 (2.7)	17.7 (2.8)	< 0.01*
%SaO ₂	97.9 (0.7)	97.9 (0.6)	0.72
PaO ₂ (mmHg)	93 (9)	96 (7)	0.34
PaCO ₂ (mmHg)	36 (2)	33 (3)	< 0.01*
pH	7.43 (0.02)	7.39 (0.07)	< 0.05*
AaDO ₂ (mmHg)	15 (7)	13 (6)	0.55
V_D/V_T	0.36 (0.04)	0.37 (0.07)	0.82
Blood lactate (mmol/L)	1.5 (0.7)	4.4 (1.8)	< 0.01*
K ⁺ (mmol/L)	3.83 (0.20)	3.90 (0.22)	0.28
	Pooled (n = 30 paired samples per variable)		
<i>Exercise above ventilatory threshold</i>	<i>Incremental exercise protocol</i>	<i>Constant workload protocol</i>	p Value
$\dot{V}O_2$ (L/min)	1.91 (0.45)	1.91 (0.44)	0.60
$\dot{V}A$ (L/min)	31.5 (8.8)	31.1 (9.7)	0.57
$\dot{V}CO_2$ (L/min)	2.15 (0.56)	1.92 (0.59)	< 0.01*
RER	1.13 (0.09)	1.00 (0.16)	< 0.01*
Tidal volume (L/breath)	1.9 (0.5)	1.9 (0.40)	0.23
Respiratory rate (breaths/min)	32.0 (5.6)	34.6 (5.4)	< 0.01*
%SaO ₂	97.8 (0.6)	97.5 (0.7)	< 0.05*
PaO ₂ (mmHg)	100 (7)	96 (11)	< 0.05*
PaCO ₂ (mmHg)	37 (3)	34 (4)	< 0.01*
pH	7.39 (0.04)	7.37 (0.08)	< 0.05*
AaDO ₂ (mmHg)	15 (5)	19 (7)	< 0.01*
V_D/V_T	0.20 (0.05)	0.21 (0.04)	0.15
Blood lactate (mmol/l)	5.3 (2.1)	6.7 (3.0)	< 0.01*
K ⁺ (mmol/L)	5.20 (0.57)	5.18 (0.61)	0.81

Mean (SD). The maximal difference in $\dot{V}O_2$ between any paired sample at rest or during exercise was 100 ml/min. The paired samples were matched at similar $\dot{V}O_2$'s that ranged from 0.28 L/min to 0.53 L/min at rest. The paired samples were matched at similar $\dot{V}O_2$'s that ranged from 1.35 to 2.87 L/min during exercise that was above the ventilatory threshold. The constant workload exercise was about 75% of peak power output from the incremental exercise test. The p value was calculated from a two-tailed, paired *t* test.

*the variable is statistically significant between protocols.

FIGURE 2. Minute by minute responses of several parameters in arterial blood in both exercise protocols in obese subjects with extreme obesity. Filled circles = First bout of exercise, the incremental exercise protocol to volitional exhaustion; Open circles = Second bout of exercise, constant workload protocol, at 75% of peak power output. PaO_2 = arterial oxygen pressure, AaDO_2 = alveolar to arterial oxygen pressure difference, PaCO_2 = arterial carbon dioxide pressure, % SaO_2 = arterial oxyhemoglobin saturation, V_D/V_T = physiological dead space to tidal volume ratio. Standard error bars are included. $n = 11$ subjects. From rest to the end of exercise in each protocol, PaO_2 increased by ~ 10 mmHg ($p < 0.05$), blood lactate increased by ~ 7 mmol/L ($p < 0.05$) and V_D/V_T decreased by ~ 0.17 ($p < 0.05$). There was no difference in the change between rest and the end of exercise between protocols for PaO_2 , V_D/V_T , or blood lactate ($p > 0.05$). The AaDO_2 , % SaO_2 , and PaCO_2 show no change from rest to peak exercise within or between each protocol ($p > 0.05$).

FIGURE 3. Responses of several cardiopulmonary parameters in both exercise protocols in extremely obese subjects. Filled circles = First bout of exercise, the incremental exercise protocol to volitional exhaustion; Open circles = Second bout of exercise, constant workload protocol at 75% of peak power output. V_T = tidal volume, $\dot{V}_E$ = minute ventilation, $\dot{V}_A$ = alveolar ventilation, HR = heart rate, RER = respiratory exchange ratio, RR = respiratory rate. Mean $\pm$ SEM, $n = 11$ subjects.

FIGURE 4. Linear regressions of the main pulmonary gas exchange variables between the two exercise protocols matched for the same $\dot{V}O_2$ in morbidly obese subjects. The incremental exercise protocol was first, and then 40 minutes later the constant workload exercise protocol was followed. Since the mean absolute difference for each of the variables presented was similar at rest and during exercise between the two protocols, the resting data ($n = 10$ pairs per panel) and the exercise data ($n = 30$ pairs per panel) were combined. PaO₂ = arterial oxygen pressure, AaDO₂ = alveolar to arterial oxygen pressure difference, PaCO₂ = arterial carbon dioxide pressure, %SaO₂ = arterial oxyhemoglobin saturation, V_D/V_T = physiological dead space to tidal volume ratio, $\dot{V}A$ = alveolar ventilation. Standard error bars are included. $n = 11$ subjects.

Table 4. Absolute difference in pulmonary gas exchange variables measured at the same $\dot{V}O_2$ between the maximal incremental protocol and constant workload protocol, including rest.

	Pooled (n = 40 paired samples per variable)		
	Mean absolute difference between incremental exercise and constant workload exercise	Absolute range	95% C.I.
$\dot{V}O_2$ (L/min)	0.04 (0.03)	0.0 to 0.1	0.03, 0.05
$\dot{V}A$ (L/min)	3.0 (3.2)	0.0 to 13.0	2.0, 4.0
$\dot{V}CO_2$ (L/min)	0.19 (0.19)	0.01 to 0.80	0.13, 0.25
RER	0.12 (0.10)	0.01 to 0.46	0.09, 0.15
Tidal volume (L/breath)	0.18 (0.17)	0.0 to 0.80	0.13, 0.23
Respiratory rate (breaths/min)	3.8 (3.3)	0.3 to 14.1	2.8, 4.8
%SaO ₂	0.5 (0.5)	0.0 to 2.1	0.4, 0.7
PaO ₂ (mmHg)	9 (7)	1.1 to 26.5	6, 11
PaCO ₂ (mmHg)	4 (2)	0 to 10	3, 4
pH	0.04 (0.06)	0.00 to 0.20	0.02, 0.06
AaDO ₂ (mmHg)	7 (6)	1 to 20	5, 8
V_D/V_T	0.04 (0.04)	0.00 to 0.18	0.03, 0.05
Blood lactate (mmol/l)	2.2 (1.7)	0 to 6.9	1.7, 2.7
K ⁺ (mmol/L)	0.3 (0.3)	0.0 to 1.3	0.2, 0.4

Mean (SD). The constant workload exercise was about 75% of peak power output from the incremental exercise test. The 95% confidence interval (95% CI) was calculated as the mean absolute difference $\pm$ 1.96 multiplied by the standard error of the mean. The variables collected at rest before each exercise protocol was combined with the variables collected during exercise since the mean absolute.

straint, the decrease in PaCO₂ in recovery would not have been seen. This suggests breathing was compromised during the first bout of exercise in subjects with extreme obesity. Intense exercise generally does not reduce the PaCO₂ in obese subjects with extreme obesity,^{5,7} while weight loss improves their exercise hyperventilation.⁷ Thus, the unexpected reduction in PaCO₂ from prior exercise in extremely obese subjects without weight loss is an exciting finding.

As prior intense exercise caused a reduction in PaCO₂ at rest by about 3 mmHg, and that the reduction was maintained when the second bout of intense exercise occurred, this suggests that the improvement in breathing occurred during recovery after the maximal incremental protocol. Evidence to support improved breathing occurred during recovery stems from the lack of change in PaCO₂ between rest and end of exercise in either bout. The reduction in PaCO₂ oc-

curred during recovery after the maximal incremental protocol.

It is well known among respiratory physiologists that impaired diffusion, right-to-left shunting and ventilation-perfusion mismatching affects AaDO₂, but pure hypoventilation does not. With pure hypoventilation, the alveolar oxygen pressure drops equally with the drop in arterial oxygen pressure, leaving the total AaDO₂ unchanged. Since AaDO₂ during recovery was not different compared to the resting value before the first bout of exercise, the mechanism for the reduced PaCO₂ and increased PaO₂ during recovery was improved hyperventilation. The slight increase in the respiratory rate associated with the metabolic acidosis during the recovery period supports the notion that hyperventilation was augmented in recovery. It would seem that the mechanical constraint of abdominal fat surrounding the chest wall can be overcome by increasing the respiratory rate in these subjects.

Limitations

There are limitations to this study. First, data obtained using a ramp-like protocol was compared with that obtained using a constant workload protocol. Two identical constant workload protocols for the research design would have allowed stronger comparisons; however, this would have required testing on two different days which would have complicated the recruiting and retaining of subjects. The use of a ramp protocol allowed us to measure power output that could be sustained for five minutes, thus $\dot{V}O_{2peak}$ was calculated and compared with power output for the constant workload protocol. About 80% of the peak power output measured from a $\dot{V}O_{2peak}$ is sustainable for five minutes⁸ and so the data from the $\dot{V}O_{2peak}$ test was used to determine the power output for the constant workload protocol. Thus, the $\dot{V}O_{2peak}$ test was used both as the first bout of exercise and for determination of the power output for the constant workload protocol. Nonetheless, having two different exercise protocols does not invalidate the findings since it was NOT the second bout of exercise *per se* that reduced the $PaCO_2$ but it was the recovery period following the first bout of exercise that reduced the $PaCO_2$. As the results demonstrate, the $PaCO_2$ during the recovery period from the first bout of exercise was 3 mmHg lower compared with the resting period prior to the first bout of exercise. This difference in $PaCO_2$ between the recovery period and the second bout of exercise did not appreciably change, suggesting the increased arterial lactate during recovery period was responsible for the reduction in $PaCO_2$ and not the second bout of exercise itself. Thus, the type of protocol for the second bout of exercise is irrelevant.

Second, the RER was higher at peak exercise in the first bout, but not in the second bout, which may be considered an issue. The measured RER generally increases above 1.00 during exhaustive exercise because buffering acids adds extra non-metabolic-

created CO_2 to the expired air above the quantity normally released during energy metabolism. After repeated bouts of exhaustive exercise, the RER can drop. The cells and bodily fluids retain CO_2 to replenish the sodium bicarbonate that buffered the accumulating lactate and this action to replenish alkaline reserve decreases the expired CO_2 level without affecting $\dot{V}O_2$.²² The drop in RER from the first to the third set of exhaustive cycling exercise is seen elsewhere in published literature;⁸ therefore, it is normal to have a low RER (lower than 1.10) when repeated exhaustive exercise is followed.

As shown by Zeballos and Weisman¹⁰ and the current study, prior intense exercise usually decreases $PaCO_2$ ⁹ resulting in a lower $PaCO_2$ in the second bout of exercise in comparison with the first;^{8,9} although this finding is not consistent.^{11,12}

Clinical Implications

This paper demonstrates that intense exercise increases arterial lactate concentration in individuals with extreme obesity, which stimulates breathing to reduce $PaCO_2$. While statistically significant, one must ask if a 3 mmHg decrease in $PaCO_2$ is clinically relevant. Given that the drop in $PaCO_2$ from rest to peak exercise in normal, non-obese individuals is about 6 mmHg,¹⁻³ the reduction in $PaCO_2$ in extremely obese individuals during the recovery period by 3 mmHg would seem to be clinically relevant. If it is subsequently found in such obese individuals that their breathing “feels” better during the recovery period after intense exercise, then these individuals might benefit from an intense, 5 min warm-up ($\geq$ ventilatory threshold) 10 to 15 minutes before exercise to promote metabolic acidosis. The warm-up would stimulate peripheral and central chemoreceptors to enhance hyperventilation during exercise and thereby improve oxygen kinetics.²³ Thus, a faster rise in oxygen uptake from prior exercise would improve ATP production though aerobic rather than anaerobic

sources, thus postponing fatigue and promoting a better exercise experience.

In conclusion, prior intense exercise causes a reduction in PaCO_2 at rest by approximately 3 mmHg. This reduction is maintained when a second bout of intense exercise is undertaken. The change in PaCO_2 from rest to end of exercise is negligible in both protocols, suggesting that the improvement in breathing occurred during recovery. It would seem that obese subjects, given a sufficient chemical stimulus, will attempt to breathe more, although this does not mean more alveolar ventilation, which is the means of removing CO_2 . Furthermore, CW exercise in obese subjects predicts $\dot{V}_A$, % SaO_2 , $\dot{V}_D/\dot{V}_T$, and PaCO_2 , but not PaO_2 or AaDO_2 during incremental exercise at a similar metabolic rate.

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