Corrected End-Tidal P_{CO_2} Accurately Estimates P_{aCO_2} at Rest and During Exercise in Morbidly Obese Adults

Vipa Bernhardt, PhD; Santiago Lorenzo, PhD; Tony G. Babb, PhD;
and Gerald S. Zavorsky, PhD

Background: Obesity affects lung function and gas exchange and imposes mechanical ventilatory limitations during exercise that could disrupt the predictability of P_{aCO_2} from end-tidal P_{CO_2} (P_{ETCO_2}), an important clinical tool for assessing gas exchange efficiency during exercise testing. P_{aCO_2} has been estimated during exercise with good accuracy in normal-weight individuals by using a correction equation developed by Jones and colleagues ($P_{JCO_2} = 5.5 + 0.9 \times P_{ETCO_2} - 2.1 \times \text{tidal volume}$). The purpose of this project was to determine the accuracy of P_{aCO_2} estimations from P_{ETCO_2} and P_{JCO_2} values at rest and at submaximal and peak exercise in morbidly obese adults.

Methods: P_{aCO_2} and P_{ETCO_2} values from 37 obese adults (22 women, 15 men; age, 39 ± 9 y; BMI, 49 ± 7 ; [mean $\pm$ SD]) were evaluated. Subjects underwent ramped cardiopulmonary exercise testing to volitional exhaustion. P_{ETCO_2} was determined from expired gases simultaneously with temperature-corrected arterial blood gases (radial arterial catheter) at rest, every minute during exercise, and at peak exercise. Data were analyzed using paired t tests.

Results: P_{ETCO_2} was not significantly different from P_{aCO_2} at rest ($P_{ETCO_2} = 37 \pm 3$ mm Hg vs $P_{aCO_2} = 38 \pm 3$ mm Hg, $P = .14$). However, during exercise, P_{ETCO_2} was significantly higher than P_{aCO_2} (submaximal: 42 ± 4 vs 40 ± 3 , $P < .001$; peak: 40 ± 4 vs 37 ± 4 , $P < .001$, respectively). Jones' equation successfully corrected P_{ETCO_2} , such that P_{JCO_2} was not significantly different from P_{aCO_2} (submax: $P_{JCO_2} = 40 \pm 3$, $P = .650$; peak: 37 ± 4 , $P = .065$).

Conclusion: P_{JCO_2} provides a better estimate of P_{aCO_2} than P_{ETCO_2} during submaximal exercise and at peak exercise, whereas at rest both yield reasonable estimates in morbidly obese individuals. Clinicians and physiologists can obtain accurate estimations of P_{aCO_2} in morbidly obese individuals by using P_{JCO_2} .

CHEST 2013; 143(2):471–477

Abbreviations: P_{ECO_2} = partial pressure of mixed expired CO_2 ; $P(ET - a)CO_2$ = difference between end-tidal and P_{aCO_2} ; P_{ETCO_2} = partial pressure of end-tidal CO_2 ; $P(J - a)CO_2$ = difference between Jones-corrected and P_{aCO_2} ; P_{JCO_2} = estimated P_{aCO_2} with Jones correction; SEE = SE of estimates; V_{DM} = mechanical dead space; $V_D/V_T(\text{art})$ = dead space to tidal volume ratio using P_{aCO_2} ; $V_D/V_T(ET)$ = dead space to tidal volume ratio using end-tidal P_{CO_2} ; $V_D/V_T(J)$ = dead space to tidal volume ratio using Jones' corrected end-tidal P_{CO_2} ; $\dot{V}O_2$ = oxygen uptake; $\dot{V}O_{2\text{peak}}$ = peak oxygen uptake at peak exercise; V_T = tidal volume

Measurements of arterial blood gases are important in studies of ventilatory control during exercise and can give valuable information about the efficiency of ventilation and gas exchange. To avoid the invasive procedure of placing arterial catheters for sampling arterial blood, partial pressure of end-tidal CO_2 (P_{ETCO_2}) has been used as a noninvasive method to estimate P_{aCO_2} in young, healthy adults at rest and during exercise.^{1–4} These studies have concluded that, although P_{ETCO_2} may slightly underestimate P_{aCO_2} at rest, P_{ETCO_2} is a good index of P_{aCO_2} during resting conditions. During exercise, the instantaneous P_{aCO_2}

fluctuates cyclically with breathing⁵ and the P_{ETCO_2} is higher than the average P_{aCO_2} over the complete breathing cycle.⁶ Therefore, P_{ETCO_2} may overestimate P_{aCO_2} during exercise, when CO_2 production, ventilation, and tidal volume (V_T) are all increased.⁷ To circumvent this problem, Jones et al³ developed a regression equation to predict P_{aCO_2} from P_{ETCO_2} (P_{JCO_2}) and V_T that corrects for the overestimation of P_{aCO_2} by P_{ETCO_2} :

$$P_{JCO_2} = 5.5 + 0.9 \times P_{ETCO_2} - 2.1 \times V_T \quad (\text{Equation 1})$$

where V_T is in liters.

This noninvasive estimation of PaCO_2 from PETCO_2 facilitates the use of repeated measures wherein the risks associated with an arterial puncture are eliminated. Studies have shown that PJCO_2 appears to be a good predictor of PaCO_2 during exercise in young adults.^{3,4,8,9} In contrast to younger individuals, the use of the Jones equation in older subjects significantly underestimated PaCO_2 at maximal exercise, whereas PETCO_2 was a better estimator of PaCO_2 .⁸ Aging is associated with changes in respiratory function, such as increased dead space (VD) and ventilation-perfusion mismatch, which may alter the relationship between PETCO_2 and PaCO_2 . Likewise, obesity is associated with changes in respiratory mechanics that may predispose otherwise healthy obese adults to abnormalities such as low lung-volume breathing and impaired gas exchange (ie, mismatch of ventilation and perfusion).¹⁰ Therefore, these respiratory changes in obesity may also affect PETCO_2 and PaCO_2 differently.

Another measurement important in studies of ventilatory control, adequacy of ventilation, and gas exchange efficiency is determination of the degree of matching of ventilation to perfusion, which can be estimated by calculating the dead space to tidal volume ratio, or VD/VT .⁶ The standard method of calculating arterial VD/VT ($\text{VD}/\text{VT}[\text{art}]$) includes measurements of PaCO_2 , partial pressure of mixed expired CO_2 (PECO_2), and a correction for apparatus dead space ($\text{VDM} = 0.95 \text{ L}$; model 2700; Hans Rudolph, Inc):

$$\frac{V_D}{V_T}(\text{art}) = \frac{PaCO_2 - P_ECO_2}{PaCO_2} - \frac{V_{DM}}{V_T} \quad (\text{Equation 2})$$

Normal values for VD/VT in healthy individuals under the age of 40 years fall from 0.29 ± 0.06 at rest to approximately 0.16 ± 0.04 at maximal exercise.⁶

The purpose of the present study was to determine the usefulness of PETCO_2 and PJCO_2 to estimate PaCO_2

at rest and during exercise in morbidly obese patients ($\text{BMI} > 40$). Obesity affects resting lung function and breathing pattern and imposes mechanical ventilatory limitations during exercise,¹¹⁻¹⁵ such that PJCO_2 may not be an applicable estimate of PaCO_2 . Furthermore, it was sought to determine if PETCO_2 or PJCO_2 could be used to predict VD/VT ($\text{VD}/\text{VT}[\text{ET}]$ and $\text{VD}/\text{VT}[\text{J}]$, respectively) by substituting either variable for PaCO_2 in Equation 2. The validity of Jones et al's³ correction equation has not been investigated in morbidly obese individuals, an increasingly prevalent clinical population for whom shortness of breath on exertion is frequently documented and, thus, cardiopulmonary exercise testing is frequently performed. Other data from this study have been published previously that addressed the sex differences in alveolar-to-arterial oxygen pressure tension.¹⁶

MATERIALS AND METHODS

Subjects

Twenty-two morbidly obese women and 15 morbidly obese men who were scheduled for laparoscopic gastric bypass surgery were recruited from a bariatric clinic to perform a graded exercise test on a cycle ergometer (19 women and 14 men) or treadmill (three women and one man) with temperature-corrected arterial blood-gas samples taken at rest and every minute of exercise, including peak exercise. Exclusion criteria for the population of morbidly obese subjects were (1) $\text{BMI} \geq 75 \text{ kg/m}^2$; (2) a medical contraindication to exercise testing; (3) heart, respiratory, renal, or hepatic failure; (4) metastatic disease; (5) senility, Alzheimer disease, or other dementias; and (6) inability to comprehend the instructions during tests. All subjects signed an informed consent form. This study was approved by the institutional review board of the McGill University Health Center (GEN#04-053).

Peak Aerobic Capacity Test

Peak aerobic capacity ($\dot{V}_{O_2\text{peak}}$) was assessed with an electrically braked cycle ergometer (Velotron Dynafit Pro; RaceMate Inc). The $\dot{V}_{O_2\text{peak}}$ test commenced at 5 W and increased by 1 W every 2 to 6 s (10-30 W/min) until volitional exhaustion. The difference in the incremental increase in power output was to make sure both men and women fatigued within 8 to 12 min. A modified Bruce protocol on a treadmill was used for patients who were unable to use a cycle ergometer because of knee and/or hip and/or lower back pain.

Minute ventilation, breathing frequency, VT , oxygen consumption ($\dot{V}_{O_2}$), CO_2 production, PETCO_2 , PECO_2 , and concentration were assessed with a metabolic cart (model VMax 229LV; CareFusion Corporation) using the breath-by-breath mode. The mean of the highest three consecutive $\dot{V}_{O_2}$ values (averaged over 20-s intervals) was defined as the $\dot{V}_{O_2\text{peak}}$.

Arterial Catheterization

Arterial catheterization of the radial artery was performed as described previously.¹⁶ Briefly, 15 min prior to the $\dot{V}_{O_2\text{peak}}$ test a rapid-response thermocouple was positioned in the hub of the radial artery catheter. The catheter and extension were routinely flushed with heparinized saline. Prior to each arterial blood gas

Manuscript received April 5, 2012; revision accepted July 1, 2012.

Affiliations: From the Institute for Exercise and Environmental Medicine (Drs Bernhardt, Lorenzo, and Babb), Texas Health Presbyterian Hospital Dallas and University of Texas Southwestern Medical Center, Dallas, TX; and McGill University Health Centre (Dr Zavorsky), Montreal, QC, Canada.

Dr Zavorsky is currently affiliated with the Human Physiology Laboratory, Marywood University and The Commonwealth Medical College (Scranton, PA).

Funding/Support: The study was funded by the Fonds de la Recherche en Santé du Québec, National Institutes of Health [Grant HL096782], and the Wallace Barbara and Kelly King Charitable Foundation Trust.

Correspondence to: Tony G. Babb, PhD, Institute for Exercise and Environmental Medicine, 7232 Greenville Ave, Ste 435, Dallas, TX 75231; e-mail TonyBabb@TexasHealth.org

© 2013 American College of Chest Physicians. Reproduction of this article is prohibited without written permission from the American College of Chest Physicians. See online for more details.

DOI: 10.1378/chest.12-0896

sample, 5 mL of arterial blood was rapidly withdrawn to eliminate dead space and for measurement of arterial blood temperature. Immediately after the 5-mL withdrawal, another 2 mL was withdrawn for actual blood gas analysis using a special syringe (arterial blood sample syringe with dry lithium heparin for gases and electrolytes; Smiths Medical). These blood gas samples were withdrawn over a 10-s period to reduce the fluctuations of blood gas tensions over a given respiratory cycle. Arterial blood gases were measured after 5 min of rest, with the subjects sitting upright on a chair. The average of duplicate samples was recorded. Arterial blood gases were also measured every minute throughout exercise and at peak exercise (right at volitional exhaustion from the $\dot{V}_{O_{2peak}}$ test). The formula for temperature-corrected P_{aCO_2} value is based on section 4.3.2 in the guidelines of the Clinical Laboratory Standards Institute.¹⁷

Statistical Analyses

Independent *t* tests were used to compare body measurements, pulmonary function, cardiopulmonary, and arterial blood gas parameters between sexes at rest and during exercise. Paired *t* tests were used to determine whether significant differences existed between measured P_{aCO_2} and estimated P_{aCO_2} ($PETCO_2$ and $PJCO_2$) at rest, at 4 min during exercise (submaximal effort), and at peak exercise within each subject. The 4 min point was chosen based on the total duration of the test, which lasted 10 min on average. Linear regression analysis was used to assess the relationship between P_{aCO_2} and $PETCO_2$. A Bland-Altman analysis was used to determine the bias and error between the measurements of P_{aCO_2} and $PJCO_2$. A *P* value < .05 was considered statistically significant. All results are expressed as mean $\pm$ SD. Data were analyzed using SigmaStat for Windows 11.0 (Systat Software).

RESULTS

Subject characteristics, spirometry, and lung diffusion capacity measurements are shown in Table 1. One-third of subjects had a diagnosis of obstructive sleep apnea. Sixty percent of subjects had never smoked, 30% stopped smoking 2 to 12 years ago, and 10% were current smokers (10 cigarettes per day). Respiratory variables obtained at rest and peak exercise are shown in Table 2.

No significant differences were found between men and women in P_{aCO_2} , $PETCO_2$, or $PJCO_2$ values at rest, submaximal exercise, or peak exercise (*P* > .05, data not shown) and were combined in further analyses. A linear regression of 320 pairs of P_{aCO_2} and $PJCO_2$ at rest and throughout exercise revealed a correlation coefficient of *r* = 0.83 (adjusted *r*² = 0.73, SE of estimates [SEE] = 1.86 mm Hg, *P* < .001) (Fig 1). A Bland-Altman plot shows the agreement between P_{aCO_2} and $PJCO_2$ (Fig 2) with a bias of 0.2 mm Hg and SEE = 1.7.

Mean values of P_{aCO_2} , $PETCO_2$, and $PJCO_2$ are shown in Figure 3 and mean differences between measured P_{aCO_2} and $PETCO_2$ (ie, $P[ET - a]CO_2$) and P_{aCO_2} and $PJCO_2$ (ie, $P[J - a]CO_2$) in Figure 4. At rest, $PETCO_2$ was not significantly different from P_{aCO_2} (*P* = .138). However, at submaximal and peak exercise, $PETCO_2$ was significantly higher than P_{aCO_2} (submaximal: $P[ET - a]CO_2 = 2.4 \pm 2.0$ mm Hg, *P* < .001; peak: $P[ET - a]CO_2 = 2.3 \pm 1.9$ mm Hg, *P* < .001). The Jones equation successfully corrected $PETCO_2$, such that $PJCO_2$ was not significantly different from P_{aCO_2} (submaximal: $P[J - a]CO_2 = 0.1 \pm 1.9$ mm Hg, *P* = .650; peak: $P[J - a]CO_2 = -0.6 \pm 1.8$ mm Hg, *P* = .065). Eliminating the four subjects who performed the exercise on the treadmill did not change the significance of these results (data not shown). The prevalence of exercise-induced hypoxemia (about 11% of subjects with P_{aO_2} < 80 mm Hg) and gas exchange impairments (about 18% of subjects with alveolar-arterial oxygen tension difference > 25 mm Hg) at peak exercise was rare and was previously published.¹⁸ No correlation between subjects' age and $P(ET - a)CO_2$ or $P(J - a)CO_2$ were found (data not shown).

Figure 5 shows the measured arterial V_D/V_T ($V_D/V_T[art]$) and estimated $V_D/V_T(ET)$ and $V_D/V_T(J)$ ratios at rest and during exercise. At rest, none of the ratios were significantly different from each other (*P* > .05). With increasing $\dot{V}_{O_2}$, $V_D/V_T(ET)$ did not decrease as much as $V_D/V_T(art)$ and $V_D/V_T(J)$ and was significantly higher at submaximal and peak exercise (*P* < .001). $V_D/V_T(J)$ was not significantly different from $V_D/V_T(art)$ at all work rates (*P* > .05). $P(ET - a)CO_2$ was closely correlated with $V_D/V_T(art)$ (*r* = -0.76, *P* < .001) (Fig 5).

DISCUSSION

These data are the first to suggest that $PJCO_2$ provides a better estimate of arterial P_{aCO_2} than $PETCO_2$ in morbidly obese subjects during submaximal exercise as well as at peak exercise, indicating that $PJCO_2$ can be used to accurately estimate P_{aCO_2} in morbidly obese men and women. At rest, both $PJCO_2$ and $PETCO_2$ provide reasonable estimates of P_{aCO_2} (Figs 3, 4). $V_D/V_T(art)$ was accurately estimated using the $PJCO_2$ in place of P_{aCO_2} in the calculation. Our results are of practical clinical importance as the prevalence of obesity and morbid obesity is consistently increasing.¹⁹

Table 1—Subject Characteristics

Subjects	Age, y	Height, cm	Weight, kg	BMI, kg/m ²	FVC, % pred	FEV ₁ , % pred	FEV ₁ /FVC	DLCO, % pred
Women	37 $\pm$ 10	164 $\pm$ 7	134.0 $\pm$ 16.8	50.0 $\pm$ 5.1	99 $\pm$ 14	91 $\pm$ 14	75 $\pm$ 7	99 $\pm$ 13
Men	41 $\pm$ 8	178 $\pm$ 7	153.9 $\pm$ 29.0	48.6 $\pm$ 8.6	95 $\pm$ 14	92 $\pm$ 16	77 $\pm$ 6	95 $\pm$ 11

Data presented as mean $\pm$ SD. DLCO = diffusing capacity for carbon monoxide; pred = predicted.

Table 2—Respiratory Variables at Rest and Peak Exercise

Measurement Taken	$\dot{V}E$, L/min	V_T , L	f_b , bpm	$\dot{V}O_2$, L/min	$\dot{V}CO_2$, L/min
Rest					
Women	11.1 ± 2.1	0.71 ± 0.13	16 ± 3	0.33 ± 0.04	0.28 ± 0.04
Men	13.5 ± 2.7^a	0.90 ± 0.30^a	16 ± 3	0.42 ± 0.08^a	0.35 ± 0.07^a
Peak exercise					
Women	68.5 ± 17.5	1.76 ± 0.47	40 ± 6	1.92 ± 0.38	2.25 ± 0.49
Men	90.4 ± 21.6^a	2.43 ± 0.44^a	37 ± 7	2.57 ± 0.57^a	2.94 ± 0.62^a

Data presented as mean $\pm$ SD. bpm = breaths per minute; f_b = breathing frequency; $\dot{V}CO_2$ = rate of CO_2 production; $\dot{V}E$ = minute ventilation; $\dot{V}O_2$ = rate of O_2 consumption; V_T = tidal volume.

^a $P < .01$ significantly different from women.

This population often presents with shortness of breath on exertion, and thus cardiopulmonary exercise testing is frequently performed. The use of the noninvasive, corrected $PETCO_2$ measure can save patient discomfort, time, and cost.

$PETCO_2$ is an acceptable estimate for $PaCO_2$ at rest in younger, nonobese subjects.¹⁻⁴ Extreme obesity is associated with changes in respiratory mechanics and gas exchange properties that may disturb the relationship between $PaCO_2$ and $PETCO_2$. However, based on our findings in morbidly obese subjects, the $P(ET - a)CO_2$ differences at rest and during exercise were small and well within the previously published ranges,¹⁻⁴ confirming that although obesity places a substantial load on the respiratory system, which could affect gas exchange kinetics, it does not affect CO_2 clearance.²⁰

During resting conditions, our results showed that $PETCO_2$ was not significantly different from $PaCO_2$ ($P[ET - a]CO_2 = -0.5 \pm 2.2$ mm Hg), which is consistent with previous investigations in which $PETCO_2$ has been reported to underestimate $PaCO_2$ by 0.3,³ 0.7,⁸ 1.4,⁴ and 2.8 mm Hg.² The slightly lower $PETCO_2$ at rest in those normal-weight individuals was attributed to dilution by gas from poorly perfused apical alveoli.³

During exercise, $PETCO_2$ has been found to increase up to 4 mm Hg above $PaCO_2$.¹ Our data also demonstrated an overestimation of $PETCO_2$, up to 2.4 ± 2.0 mm Hg during exercise, which was significantly greater than $PaCO_2$. $PETCO_2$ exceeds $PaCO_2$ during exercise due to the increased CO_2 production and delivery to the lungs⁶ and the decreasing volume of alveolar air throughout exhalation,²¹ resulting in a continued increase of $PaCO_2$ during exhalation. $PETCO_2$ is measured as the highest instantaneous $PaCO_2$ at the end of expiration, whereas the measurement of $PaCO_2$ represents the average $PaCO_2$ during the entire respiratory cycle. In addition, cardiac output and pulmonary blood flow are increased during exercise,

FIGURE 1. Linear regression (solid line) and 95% prediction intervals (dotted lines) between 320 pairs of $PaCO_2$ and P_jCO_2 at rest and during exercise. P_jCO_2 = Jones-corrected end-tidal PCO_2 ; SEE = SE of estimates.

FIGURE 2. Bland-Altman plot of the average of $PaCO_2$ and P_jCO_2 vs their difference. $N = 311$, SEE = 1.7, bias = 0.2 mm Hg (solid line), 95% prediction limits (dashed lines). $P(j-a)CO_2$ = difference between Jones-corrected and $PaCO_2$. See Figure 1 legend for expansion of abbreviations.

FIGURE 3. Mean $\pm$ SD values of PaCO_2 , $\text{P}_{\text{ET}}\text{CO}_2$, and $\text{P}_{\text{J}}\text{CO}_2$. $\text{P}_{\text{ET}}\text{CO}_2$ significantly overestimated PaCO_2 during exercise. Jones' equation successfully corrected $\text{P}_{\text{ET}}\text{CO}_2$ such that $\text{P}_{\text{J}}\text{CO}_2$ was not significantly different from PaCO_2 . * $P < .001$ between $\text{P}_{\text{ET}}\text{CO}_2$ and PaCO_2 as well as between $\text{P}_{\text{ET}}\text{CO}_2$ and $\text{P}_{\text{J}}\text{CO}_2$. $\text{P}_{\text{ET}}\text{CO}_2$ = partial pressure of end-tidal CO_2 ; $\dot{V}_{\text{E}}$ = minute ventilation. See Figure 1 legend for expansion of other abbreviation.

resulting in better perfusion and increased PaCO_2 and PETCO_2 . Although PaCO_2 remains relatively unchanged, PaCO_2 increases, and thus $\text{P}(\text{ET} - \text{a})\text{CO}_2$ increases.²² Using a lung model simulating the cyclic nature of breathing, Benallal and Busso²³ demonstrated that a 10% simultaneous increase in CO_2 production, oxygen uptake, and cardiac output resulted in an increase in the $\text{P}(\text{ET} - \text{a})\text{CO}_2$ difference, whereas changing dead space ventilation had no influence.

From rest to peak exercise, PaCO_2 usually decreases about 5 to 6 mm Hg in normal-weight individuals.²⁴ Our data confirm that in morbidly obese subjects, PaCO_2 is maintained above 35 mm Hg (specifically, 37.6 ± 2.8 mm Hg at rest and 37.4 ± 4.4 mm Hg at

FIGURE 4. Differences (mean $\pm$ SD) between PaCO_2 and $\text{P}_{\text{ET}}\text{CO}_2$ ($\text{P}_{\text{ET}} - \text{a}$) CO_2 , as well as PaCO_2 and $\text{P}_{\text{J}}\text{CO}_2$ ($\text{P}_{\text{J}} - \text{a}$) CO_2 values. * $P < .001$ significant difference between $\text{P}_{\text{ET}} - \text{a}$) CO_2 and zero as well as between $\text{P}_{\text{ET}} - \text{a}$) CO_2 and $\text{P}_{\text{J}} - \text{a}$) CO_2 . See Figure 3 legend for expansion of abbreviations.

FIGURE 5. Mean arterial, end-tidal, and Jones-corrected $\text{V}_{\text{D}}/\text{V}_{\text{T}}$ ratios at rest, submaximal exercise, and peak exercise. * $P < .001$ significant difference between $\text{V}_{\text{D}}/\text{V}_{\text{T}}(\text{ET})$ vs $\text{V}_{\text{D}}/\text{V}_{\text{T}}(\text{art})$ and $\text{V}_{\text{D}}/\text{V}_{\text{T}}(\text{J})$. $\text{V}_{\text{D}}/\text{V}_{\text{T}}(\text{art})$ = dead space to tidal volume ratio using PaCO_2 ; $\text{V}_{\text{D}}/\text{V}_{\text{T}}(\text{ET})$ = dead space to tidal volume ratio using end-tidal $\text{P}_{\text{ET}}\text{CO}_2$; $\text{V}_{\text{D}}/\text{V}_{\text{T}}(\text{J})$ = dead space to tidal volume ratio using $\text{P}_{\text{J}}\text{CO}_2$. See Figure 1 and 3 legends for expansion of other abbreviations.

peak exercise) (Fig 3), suggesting inadequate compensatory exercise hyperventilation.^{18,25,26}

VD/VT is a measure of dead space ventilation and provides an estimate of the degree of matching of ventilation to perfusion in the lung during rest and exercise.⁶ In our obese individuals, $\text{VD}/\text{VT}(\text{art})$ at rest was elevated compared with young, nonobese subjects⁶ and was similar to values found in older men.^{8,27} During exercise, however, $\text{VD}/\text{VT}(\text{art})$ dropped to normal levels, in contrast to older men, whose values were significantly higher than in younger subjects. The decrease in VD/VT with exercise is attributed to an increased perfusion of areas of the lungs with high ventilation-perfusion ratios at rest²⁸ and a relatively greater increase in VT than anatomic dead space.¹ Ventilation-perfusion mismatching can cause PaCO_2 to exceed PETCO_2 ,²⁹ resulting in a negative $\text{P}(\text{ET} - \text{a})\text{CO}_2$ difference. During exercise, VD/VT was normal, and the $\text{P}(\text{ET} - \text{a})\text{CO}_2$ difference was positive. This suggests that ventilation-perfusion mismatching exists in morbidly obese subjects only at rest but improves with exercise so that PETCO_2 exceeds PaCO_2 , as it does in healthy nonobese individuals. Using PETCO_2 or PJCO_2 as substitutes for PaCO_2 in the calculations for VD/VT (Equation 2) showed that during exercise $\text{VD}/\text{VT}(\text{ET})$ significantly overestimated $\text{VD}/\text{VT}(\text{art})$, falsely classifying certain individuals as abnormal in terms of dead space ventilation. VD/VT was corrected by using the Jones correction, suggesting that $\text{VD}/\text{VT}(\text{J})$ could be used to estimate $\text{VD}/\text{VT}(\text{art})$ in morbidly obese subjects. The actual and estimated VD/VT values only differ in the source of the PaCO_2 term in Equation 2, but the practical applicability lies in its ready use for clinicians and physiologists to

evaluate obese patients and subjects. The use of V_D/V_T estimates in patients with respiratory disease, however, may not be appropriate.^{30,31}

One minor limitation to this study is that we do not have measures of lung volumes, only of spirometry (Table 1). Since the lung function measurements were normal (in percent predicted), some forms of chronic lung disease can be excluded. Obesity reduces some lung volumes, such as functional residual capacity and expiratory reserve volume,¹⁵ but the normal spirometry variables from our subjects suggest that lung volumes were probably not grossly abnormal.

We conclude from our data that $PjCO_2$ provides the best estimate of $PaCO_2$ during exercise in otherwise healthy, morbidly obese individuals ($BMI > 40 \text{ kg/m}^2$). Both $PjCO_2$ and $PETCO_2$ yield reasonable estimates of $PaCO_2$ at rest. In addition, $V_D/V_T(J)$ provided a closer estimate of $V_D/V_T(art)$ than $V_D/V_T(ET)$ during exercise. These results suggest that gas exchange is not appreciably altered in morbidly obese individuals. Clinicians and physicians can obtain relatively accurate estimations of $PaCO_2$ in morbidly obese individuals by using $PjCO_2$.

ACKNOWLEDGMENTS

Author contributions: Dr Zavorsky is the guarantor of this manuscript.

Dr Bernhardt: contributed to performing data analysis and contributed substantially to writing of the manuscript.

Dr Lorenzo: contributed to important development of the manuscript.

Dr Babb: contributed substantially to data interpretation and development of the manuscript.

Dr Zavorsky: contributed to planning the project; supervised data collection; assisted in data collection, data processing, and analysis; and reviewed and revised the manuscript.

Financial/nonfinancial disclosures: The authors have reported to CHEST that no potential conflicts of interest exist with any companies/organizations whose products or services may be discussed in this article.

Role of sponsors: The sponsors had no role in the design of the study, the collection and analysis of the data, or in the preparation of the manuscript.

Other contributions: We thank Allison M. Straub, BS, and Kaleen M. Lavin, BS, for their assistance in various stages of this project. This work was performed at the Montreal General Hospital at McGill University Health Center.

REFERENCES

1. Wasserman K, Van Kessel AL, Burton GG. Interaction of physiological mechanisms during exercise. *J Appl Physiol.* 1967;22(1):71-85.
2. Whipp BJ, Wasserman K. Alveolar-arterial gas tension differences during graded exercise. *J Appl Physiol.* 1969;27(3):361-365.
3. Jones NL, Robertson DG, Kane JW. Difference between end-tidal and arterial PCO_2 in exercise. *J Appl Physiol.* 1979;47(5):954-960.
4. Robbins PA, Conway J, Cunningham DA, Khamnei S, Paterson DJ. A comparison of indirect methods for continuous

- estimation of arterial PCO_2 in men. *J Appl Physiol.* 1990;68(4):1727-1731.
5. Dubois AB, Britt AG, Fenn WO. Alveolar CO_2 during the respiratory cycle. *J Appl Physiol.* 1952;4(7):535-548.
6. Wasserman K, Hansen JE, Sue DY, Stringer WW, Whipp BJ. *Principles of Exercise Testing and Interpretation.* 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005.
7. Jones NL, McHardy GJ, Naimark A, Campbell EJ. Physiological dead space and alveolar-arterial gas pressure differences during exercise. *Clin Sci.* 1966;31(1):19-29.
8. Williams JS, Babb TG. Differences between estimates and measured $PaCO_2$ during rest and exercise in older subjects. *J Appl Physiol.* 1997;83(1):312-316.
9. St Croix CM, Cunningham DA, Kowalchuk JM, et al. Estimation of arterial PCO_2 in the elderly. *J Appl Physiol.* 1995;79(6):2086-2093.
10. Barrera F, Hillyer P, Ascanio G, Bechtel J. The distribution of ventilation, diffusion, and blood flow in obese patients with normal and abnormal blood gases. *Am Rev Respir Dis.* 1973;108(4):819-830.
11. Sampson MG, Grassino AE. Load compensation in obese patients during quiet tidal breathing. *J Appl Physiol.* 1983;55(4):1269-1276.
12. Pelosi P, Croci M, Ravagnan I, et al. Respiratory system mechanics in sedated, paralyzed, morbidly obese patients. *J Appl Physiol.* 1997;82(3):811-818.
13. Koenig SM. Pulmonary complications of obesity. *Am J Med Sci.* 2001;321(4):249-279.
14. DeLorey DS, Wyrick BL, Babb TG. Mild-to-moderate obesity: implications for respiratory mechanics at rest and during exercise in young men. *Int J Obes (Lond).* 2005;29(9):1039-1047.
15. Salome CM, King GG, Berend N. Physiology of obesity and effects on lung function. *J Appl Physiol.* 2010;108(1):206-211.
16. Zavorsky GS, Christou NV, Kim J, Carli F, Mayo NE. Preoperative gender differences in pulmonary gas exchange in morbidly obese subjects. *Obes Surg.* 2008;18(12):1587-1598.
17. NCCLS. *Blood Gas and pH Analysis and Related Measurements; Approved Guideline.* Wayne, PA: NCCLS; 2001
18. Zavorsky GS, Murias JM, Kim J, Gow J, Christou NV. Poor compensatory hyperventilation in morbidly obese women at peak exercise. *Respir Physiol Neurobiol.* 2007;159(2):187-195.
19. Flegal KM, Carroll MD, Ogden CL, Curtin LR. Prevalence and trends in obesity among US adults, 1999-2008. *JAMA.* 2010;303(3):235-241.
20. Zavorsky GS, Hoffman SL. Pulmonary gas exchange in the morbidly obese. *Obes Rev.* 2008;9(4):326-339.
21. Aitken RS, Clark-Kennedy AE. On the fluctuation in the composition of the alveolar air during the respiratory cycle in muscular exercise. *J Physiol.* 1928;65(4):389-411.
22. Liu Z, Vargas F, Stansbury D, Sasse SA, Light RW. Comparison of the end-tidal arterial PCO_2 gradient during exercise in normal subjects and in patients with severe COPD. *Chest.* 1995;107(5):1218-1224.
23. Benallal H, Busso T. Analysis of end-tidal and arterial PCO_2 gradients using a breathing model. *Eur J Appl Physiol.* 2000;83(4-5):402-408.
24. Holmgren A, Linderholm H. Oxygen and carbon dioxide tensions of arterial blood during heavy and exhaustive exercise. *Acta Physiol Scand.* 1958;44(3-4):203-215.
25. Dempsey JA, Wagner PD. Exercise-induced arterial hypoxemia. *J Appl Physiol.* 1999;87(6):1997-2006.
26. Zavorsky GS, Kim J, Cass LM, Carli F. Prior intense exercise reduces arterial carbon dioxide pressure in extreme obesity. *Clin Invest Med.* 2010;33(5):E321-E334.
27. Johnson BD, Reddan WG, Pegelow DF, Seow KC, Dempsey JA. Flow limitation and regulation of functional residual capacity

- during exercise in a physically active aging population. *Am Rev Respir Dis*. 1991;143(5 pt 1):960-967.
28. West JB, Jones NL. Effects of changes in topographical distribution of lung blood flow on gas exchange. *J Appl Physiol*. 1965;20(5):825-835.
 29. Miller RM, Tenney SM. Dead space ventilation in old age. *J Appl Physiol*. 1956;9(3):321-327.
 30. Lewis DA, Sietsema KE, Casaburi R, Sue DY. Inaccuracy of noninvasive estimates of VD/VT in clinical exercise testing. *Chest*. 1994;106(5):1476-1480.
 31. Zimmerman MI, Miller A, Brown LK, Bhuptani A, Sloane MF, Teirstein AS. Estimated vs actual values for dead space/tidal volume ratios during incremental exercise in patients evaluated for dyspnea. *Chest*. 1994;106(1):131-136.