special communication

Differences between estimates and measured Pa_{CO_2} during rest and exercise in older subjects

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Williams, J. S., and T. G. Babb. Differences between estimates and measured Pa_{CO_2} during rest and exercise in older subjects. *J. Appl. Physiol.* 83(1): 312–316, 1997.—Arterial P_{CO_2} (Pa_{CO_2}) has been estimated during exercise with good accuracy in younger individuals by using the Jones equation (P_JCO_2) (*J. Appl. Physiol.* 47: 954–960, 1979). The purpose of this project was to determine the utility of estimating Pa_{CO_2} from end-tidal P_{CO_2} (PET_{CO_2}) or P_JCO_2 at rest, ventilatory threshold ($\dot{V}$Th), and maximal exercise (Max) in older subjects. PET_{CO_2} was determined from respired gases simultaneously (MGA 1100) with arterial blood gases (radial arterial catheter) in 12 older and 11 younger subjects at rest and during exercise. Mean differences were analyzed with paired *t*-tests, and relationships between the estimated Pa_{CO_2} values and the actual values of Pa_{CO_2} were determined with correlation coefficients. In the older subjects, PET_{CO_2} was not significantly different from Pa_{CO_2} at rest (-1.2 ± 4.3 Torr), $\dot{V}$Th (0.4 ± 2.5), or Max (-0.8 ± 2.7), and the two were significantly ($P < 0.05$) correlated at $\dot{V}$th ($r = 0.84$) and Max ($r = 0.87$) but not at rest ($r = 0.47$). P_JCO_2 was similar to Pa_{CO_2} at rest (-1.0 ± 3.9) and $\dot{V}$th (-1.3 ± 2.3) but significantly lower at Max (-3.0 ± 2.6), and the two were significantly correlated at $\dot{V}$th ($r = 0.86$) and Max ($r = 0.80$) but not at rest ($r = 0.54$). PET_{CO_2} was significantly higher than Pa_{CO_2} during exercise in the younger subjects but similar to Pa_{CO_2} at rest. P_JCO_2 was similar to Pa_{CO_2} at rest and $\dot{V}$th but significantly lower at Max in younger subjects. In conclusion, our data demonstrate that Pa_{CO_2} during exercise is better estimated by PET_{CO_2} than by P_JCO_2 in older subjects, contrary to what is observed in younger subjects. This appears to be related to the finding that PET_{CO_2} does not exceed Pa_{CO_2} during exercise in older subjects, as occurs in the younger subjects. However, Pa_{CO_2} at rest is best estimated by P_JCO_2 in both younger and older subjects.

aging; blood gases; arterial end-tidal carbon dioxide difference; arterial partial carbon dioxide pressure

THE MEASUREMENT OF END-TIDAL P_{CO_2} (PET_{CO_2}) has been used to estimate arterial P_{CO_2} (Pa_{CO_2}) in young subjects during rest and exercise (7, 12, 16). Although PET_{CO_2} may underestimate Pa_{CO_2} at rest, most studies of younger subjects have concluded that PET_{CO_2} represents a good index of Pa_{CO_2} at rest. However, it has been shown that PET_{CO_2} may significantly overestimate Pa_{CO_2} during exercise. The instantaneous alveolar P_{CO_2} (PA_{CO_2}) fluctuates cyclically with breathing, and the PET_{CO_2} is higher than the average PA_{CO_2} over the complete breathing cycle, particularly during exercise (3). To predict Pa_{CO_2} from PET_{CO_2} and tidal volume (VT), Jones et al. (7) developed a regression equation (P_JCO_2) that corrects for the overestimation of Pa_{CO_2} by PET_{CO_2}

$$P_JCO_2 = 5.5 + 0.9PET_{CO_2} - 2.1V_T$$

where VT is in liters.

Results demonstrated that Pa_{CO_2} was predicted to within 1.04 (±SD) Torr between 25 and 58 Torr ($r = 0.96$) in a group of younger subjects ($n = 56$). This noninvasive estimation of Pa_{CO_2} from PET_{CO_2} facilitates the use of repeated measures where the risks associated with an arterial puncture are eliminated. The purpose of the present study was to determine the utility of P_JCO_2 in older subjects by comparing differences between P_JCO_2 and measured Pa_{CO_2} during rest and exercise. Changes in respiratory function secondary to the aging process, such as increased dead space and ventilation-perfusion ($\dot{V}A/\dot{Q}$) inhomogeneity, may alter the relationship between PET_{CO_2} and Pa_{CO_2}. The Jones equation is designed to correct for the overestimation of Pa_{CO_2} by PET_{CO_2}, and during conditions of increased dead space and $\dot{V}A/\dot{Q}$ mismatching, which may occur with aging, P_JCO_2 may not be an applicable estimate of Pa_{CO_2}.

METHODS

Subjects. Volunteers were recruited through local advertisements. Subjects had no history of asthma or of musculoskeletal or cardiovascular disease. None of the subjects had participated in regular vigorous physical exercise for the last 6 mo. All details of the study were discussed with the volunteers, and informed consent was obtained in accordance with the Institutional Review Board. All qualified participants were instructed to avoid exercise, food, smoking, caffeine, and alcohol for at least 2 h before testing. All subjects were familiarized with cycle-ergometry exercise before testing.

Pulmonary function. All subjects performed standard spirometry, lung volume, and diffusing capacity determinations (model 6200 body plethysmograph, Sensormedics). Pulmonary function testing was performed in accordance with the American Thoracic Society standards (5). Also, American Thoracic Society standards were used to determine normality of pulmonary function (1). Subjects not meeting these standards were excluded from participation. Predicted values were based on norms of Knudson et al. (8) and Enright et al. (4).

Table 1. *Subject characteristics and selected pulmonary functions*

Group	n	Age, yr	Ht, cm	Wt, kg	Gender	FVC, liters	FVC, %pred	FEV_1, liters	FEV_1, %pred	TLC, liters	TLC, %pred	RV/TLC, %
Younger	11	37.9 ± 3.0	174.2 ± 2.0	74.2 ± 2.9	7M/4W	4.8 ± 0.9	105.5 ± 8.6	3.8 ± 0.8	101.4 ± 10.2	6.1 ± 1.1	95.4 ± 8.8	22.9 ± 2.6
Older	12	70.0 ± 3.0	169.2 ± 2.7	70.3 ± 3.8	6M/6W	4.2 ± 1.2	115.1 ± 17.6	2.9 ± 0.8*	103.7 ± 13.6	6.6 ± 1.4	113.8 ± 13.2*	37.1 ± 5.9*

Values are means ± SD. *n*, No. of subjects; Ht, height; Wt, weight; M, men; W, women; FVC, forced vital capacity; %pred, %predicted; FEV_1, forced expired volume in 1 s; TLC, total lung capacity; RV, residual volume. *Significantly different from younger group. $P < 0.05$.

Gas exchange measurements. O_2 uptake ($\dot{V}O_2$) and CO_2 production ($\dot{V}CO_2$) were determined with a customized gas-exchange system (NEC 486DX) on a breath-by-breath basis and averaged over 20-s intervals. Gas samples were drawn continuously at 60 ml/min from a mouthport and analyzed with a mass spectrometer (model 1100, Marquette Electronics). Expired volume was measured at the mouth with a turbine flowmeter (Interface Associates) that was calibrated before each test with a 3-liter calibration syringe. Subjects breathed through a two-way valve (model 2700, Hans Rudolph) attached distally to the turbine flowmeter. Total system dead space was 170 ml, and system resistance was <1 $cmH_2O \cdot l^{-1} \cdot s$ up to 6 l/s expiration. Validation of the automated gas-exchange system is provided by regularly performed comparisons with values obtained through the expired collection bag technique. The ECG was monitored continuously (model CS-100, Schiller), and blood pressure was monitored via an automated system (model 4240, SunTech). PET_{CO_2} values were determined and averaged from the breaths occurring during the middle 20 s of each 1-min workload up to maximal exertion. At maximal exercise, PET_{CO_2} values were also averaged over 20 s before the cessation of exercise. Standard reference gases were used to calibrate the respired gas analyzer before all testing. Care was taken to ensure that the total lung capacity (TLC) maneuver was obtained after the PET_{CO_2} determination or blood sampling period. The dead space-to-tidal volume ratio (V_{DS}/V_T) was calculated by using standard procedures and Pa_{CO_2} and averaged expired PCO_2 from the same time period.

Breathing mechanics. End-expiratory lung volume (EELV) was estimated at rest and during exercise from measurement of inspiratory capacity (IC). Measurement of IC was performed by having the subject, on cue from the investigator, inhale maximally to TLC during the last few seconds of each exercise stage. The subjects in our study were able to perform the procedure without difficulty. EELV was estimated to determine the V_T/EELV ratio (in %). EELV was expressed as a percentage of TLC (EELV/TLC%).

Blood samples. Measurements of arterial blood gases were made via an arterial catheter placed in the radial artery. The catheter was connected to an extension tube. After drawing of sample-line dead space, samples were drawn into a heparinized syringe at rest and during the middle 20 s of each exercise level during the same time frame in which the PET_{CO_2} determinations were made. At maximal exercise, the blood samples were obtained as close as possible to the time frame corresponding to the PET_{CO_2} determinations before the cessation of exercise. The samples were immediately placed in an ice bath and were subsequently analyzed (model 282, Instrumentation Laboratories). Reference gases and commercial standards were used to calibrate the blood-gas analyzer before all testing. Routine calibration of the blood-gas analyzer is also provided by participation in an external quality-control program, and the laboratory meets all standards of a clinical blood-gas laboratory.

Exercise protocol. Testing began with the subjects seated on an electronically braked cycle ergometer (model CPE 200, MedGraphics). After 3 min of baseline measurements, exercise began at 10 W for the women and 20 W for the men, with 10- or 20-W increments until exhaustion.

Data analysis. The data were analyzed with a paired *t*-test to determine whether significant differences existed between measured Pa_{CO_2} and estimated Pa_{CO_2} (PET_{CO_2} and P_JCO_2) at rest, ventilatory threshold ($\dot{V}Th$) as described by Davis (2), and maximal exercise (Max) in both younger and older subjects. The relationship between measured and estimated Pa_{CO_2} was determined by correlation coefficients. *P* values less than 0.05 were considered to be significant. Data were analyzed with the use of SAS-PC statistical software (13).

RESULTS

The physical characteristics and selected pulmonary function values of the study population are shown in Table 1. Each individual subject had normal pulmonary function as determined by a forced vital capacity (FVC) and forced expiratory volume in 1 s (FEV_1) >80% of predicted and a TLC >90% of predicted. Mean differences ± SD between measured and estimated Pa_{CO_2} values for both older and younger subjects are shown in Fig. 1. In older subjects, PET_{CO_2} was not different from

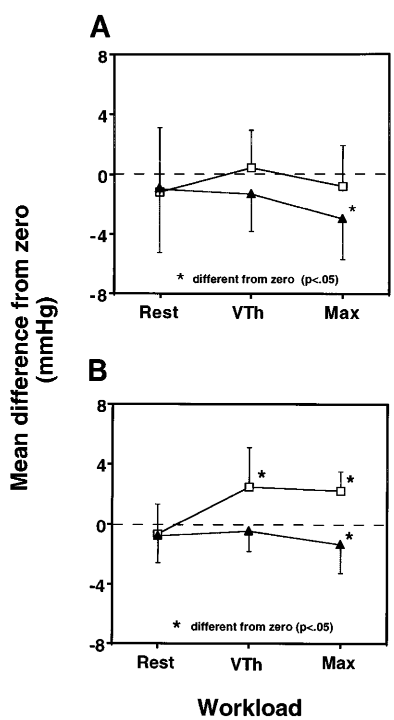

Fig. 1. Differences between directly measured (Pa_{CO_2}) and estimated arterial PCO_2 [end-tidal PCO_2 (PET_{CO_2}) and Jones-corrected PET_{CO_2} (P_JCO_2)] values for older (*A*) and younger (*B*) subjects. $\dot{V}$th, ventilatory threshold; Max, maximal exercise; □, $PET_{CO_2} - Pa_{CO_2}$; ▲, $P_JCO_2 - Pa_{CO_2}$. Values are means ± SD.

Pa_{CO_2} at rest (−1.2 ± 4.3 Torr), $\dot{V}$th (0.4 ± 2.5 Torr), or Max (−0.8 ± 2.7 Torr). P_JCO_2 was similar to Pa_{CO_2} in older subjects at rest (−1.0 ± 3.9 Torr) and $\dot{V}$th (−1.3 ± 2.3 Torr), but it was significantly lower ($P < 0.05$) at Max (−3.0 ± 2.6 Torr). In younger subjects, PET_{CO_2} was not different from Pa_{CO_2} at rest (−0.7 ± 2.0 Torr) but was significantly higher ($P < 0.05$) at $\dot{V}$th (2.5 ± 2.6 Torr) and Max (2.2 ± 1.3 Torr). P_JCO_2 was not significantly different from Pa_{CO_2} in younger subjects at rest (−0.8 ± 1.8 Torr) or $\dot{V}$th (−0.5 ± 1.3 Torr). At Max, P_JCO_2 was significantly lower ($P < 0.05$) than Pa_{CO_2} in younger subjects (−1.4 ± 1.9 Torr).

The relationship between the estimated and the actual Pa_{CO_2} values for both older and younger subjects is shown at rest, $\dot{V}$th, and Max in Fig. 2. In older subjects, PET_{CO_2} was correlated with Pa_{CO_2} ($P < 0.05$) at $\dot{V}$th ($r = 0.84$) and Max ($r = 0.87$) but not at rest ($r = 0.47$). P_JCO_2 in older subjects was also correlated with Pa_{CO_2} ($P < 0.05$) at $\dot{V}$th ($r = 0.86$) and Max ($r = 0.80$) but not at rest ($r = 0.54$). In younger subjects, PET_{CO_2} was correlated ($P < 0.05$) at rest ($r = 0.85$), $\dot{V}$th ($r = 0.81$), and Max ($r = 0.96$). P_JCO_2 was correlated with Pa_{CO_2} ($P < 0.05$) at rest ($r = 0.87$), $\dot{V}$th ($r = 0.95$), and Max ($r = 0.92$) in younger subjects. Pa_{CO_2} values were not significantly different between older and younger subjects at rest or Max; however, a difference was detected at $\dot{V}$th ($P < 0.05$).

V_{DS}/V_T was significantly higher ($P < 0.01$) at rest (0.35 ± 0.07 vs. 0.24 ± 0.04), $\dot{V}$th (0.25 ± 0.07 vs. 0.14 ± 0.04), and Max (0.26 ± 0.07 vs. 0.17 ± 0.08) for the older compared with the younger subjects, respectively. The change in V_{DS}/V_T from rest to exercise was similar for both groups.

DISCUSSION

Our results indicate that, in the older subjects we tested during exercise, PET_{CO_2} provides a better estimate of Pa_{CO_2} than does P_JCO_2. In contrast, as has been previously shown (7, 12), P_JCO_2 appears to be superior in predicting actual Pa_{CO_2} during exercise in younger

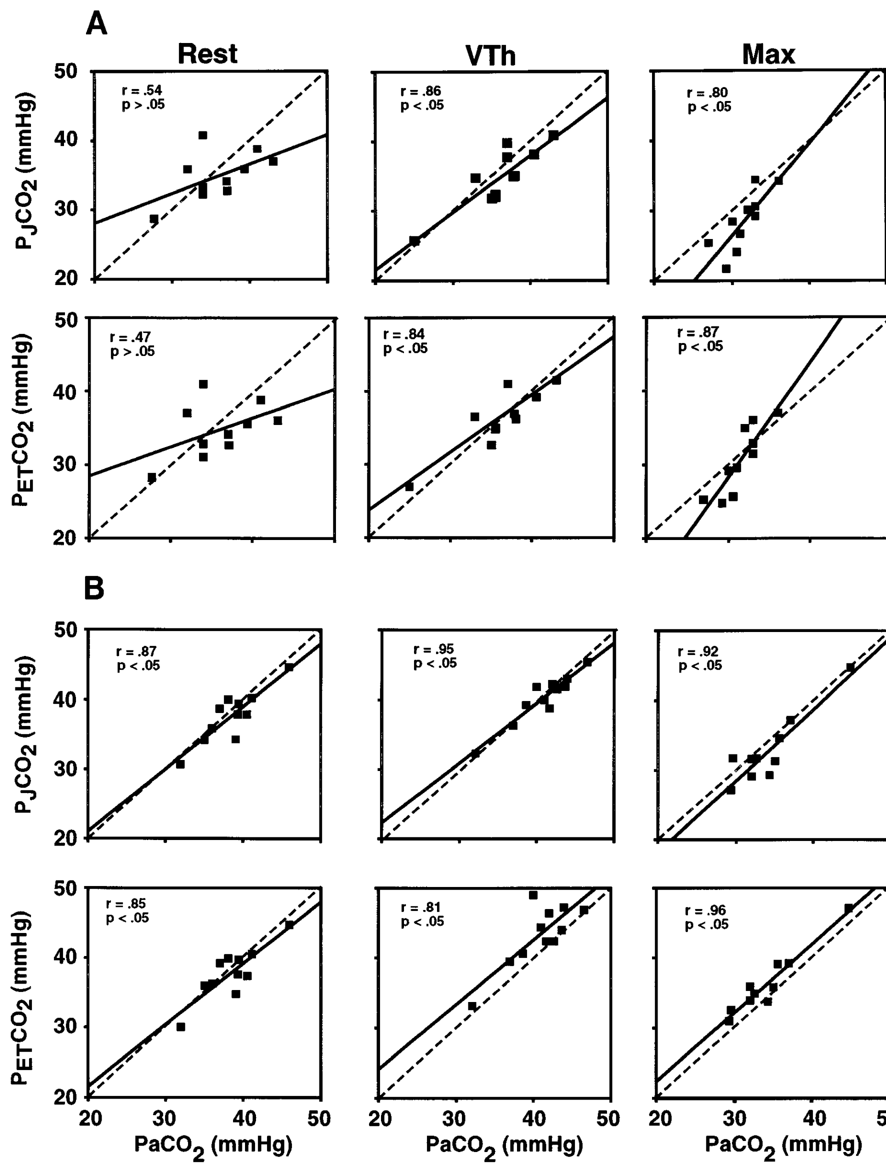

Fig. 2. Relationship between Pa_{CO_2} and 2 different methods of estimating Pa_{CO_2} in older (*A*) and younger (*B*) subjects at rest and at 2 levels of exercise (PET_{CO_2}, P_JCO_2). Dashed line, line of identity; solid line, line of best fit.

subjects. Furthermore, at rest, both P_JCO_2 and PET_{CO_2} provide reasonable estimates of Pa_{CO_2} in both groups (Fig. 1). However, in the older subjects, P_JCO_2 was better correlated to Pa_{CO_2} than was PET_{CO_2}, and both the estimates had similar correlation coefficients at rest in the younger subjects (Fig. 2).

Differences between PET_{CO_2} and Pa_{CO_2} during exercise are well documented in younger subjects (7, 12, 17). PET_{CO_2} has been shown to rise to a significantly higher value than Pa_{CO_2} during exercise. Our findings among younger subjects are consistent with these reported observations. At rest, our data showed that PET_{CO_2} was lower, though not significantly different from Pa_{CO_2} in younger subjects, also in agreement with previous reports (10, 12).

Consistent with the findings of previous investigations (7, 14) our results demonstrated that P_JCO_2 was not significantly different from Pa_{CO_2} at rest or during submaximal exercise in younger subjects. At Max, P_JCO_2 significantly underestimated Pa_{CO_2} in younger subjects. However, the mean difference was only -1.4 ± 1.9 Torr, and the two variables were strongly correlated ($r = 0.92$; $P < 0.05$).

A comparison between estimates of Pa_{CO_2} and actual Pa_{CO_2} in older adults was recently reported by St. Croix et al. (14). Pa_{CO_2} was estimated from P_JCO_2 and PET_{CO_2} at rest and during submaximal exercise (25–50 W). In contrast to our findings, these authors reported that both PET_{CO_2} and P_JCO_2 significantly overestimated Pa_{CO_2} at rest during all experimental conditions. However, measurements were made with various gas mixtures used to force PET_{CO_2} to desired values. The authors attributed these unexpected findings in part to the inspiration of hypercapnic gas mixtures, which have been shown to mask the diluting effect of the alveolar dead space on PET_{CO_2} measurements (10). Our findings at rest in older subjects revealed no significant differences between PET_{CO_2} or P_JCO_2 and Pa_{CO_2}, although both estimates were lower than measured Pa_{CO_2}. Our findings, although contrasting with those of St. Croix et al. (14) in subjects at rest, are consistent with the dilutional effects of underperfused lung apexes due to gravitational forces acting on blood flow, which causes PET_{CO_2} to be lower than Pa_{CO_2} at rest in younger subjects (10, 11). PET_{CO_2} and P_JCO_2 may even be lower at rest in an older population than values observed in younger subjects, because the “normal” decline in lung function that occurs with aging has been shown to increase alveolar dead space (15). Our findings revealed that, although neither PET_{CO_2} nor P_JCO_2 was significantly different from Pa_{CO_2} at rest in either experimental group, a slightly lower value occurred in the older subjects for both estimates.

Our findings are in partial agreement with those of St. Croix et al. (14) at submaximal exercise. During exercise, they found P_JCO_2 produced estimates that were higher than Pa_{CO_2}, although not significantly different, and PET_{CO_2} continued to significantly overestimate Pa_{CO_2}. We found no significant difference between P_JCO_2 and Pa_{CO_2} at this level of exertion in our older subjects. Our findings also revealed that PET_{CO_2} was not significantly different from Pa_{CO_2}, and, in our older subjects at submaximal exercise, PET_{CO_2} provided a better estimate of Pa_{CO_2} than did P_JCO_2.

To our knowledge, estimates of Pa_{CO_2} from P_JCO_2 have not been reported in older subjects at maximal exercise when greater CO_2 delivery to the lung results in an increased slope of the alveolar phase of the expiratory cycle (16). At Max, P_JCO_2 significantly underestimated Pa_{CO_2}, although PET_{CO_2} was not different from Pa_{CO_2} in our group of older subjects.

Several factors have been reported to determine the extent to which PET_{CO_2} differs from Pa_{CO_2} during rest and exercise (9). The fluctuation of PA_{CO_2} during the breathing cycle is one such factor (3). As VT and CO_2 increase during exercise, the variation in PA_{CO_2} during the respiratory cycle is magnified. The increased CO_2 production and decreasing lung volume as expiration continues result in PET_{CO_2} being higher than Pa_{CO_2} during exercise in young healthy subjects. Comparisons between CO_2 production for younger and older subjects in the present study revealed nonsignificant differences at rest and $\dot{V}$th ($P > 0.05$). However, CO_2 was significantly higher for younger subjects compared with the older subjects at Max ($P < 0.05$). The greater CO_2 production at Max in the younger subjects could account for the higher $PET\text{-}a_{CO_2}$ due to the effect CO_2 excretion has on the slope of the expired PA_{CO_2}.

Our observation that VT/EELV% was greater in the younger subjects appears to support the finding that PET_{CO_2} exceeds Pa_{CO_2} in younger subjects more than in the older (Fig. 3), as not only the size of the VT but the volume in which the VT mixes will affect the expired gases. Further support is provided by the finding that EELV/TLC% is greater in the older subjects and decreases less during exercise. In their study of younger subjects, Jones et al. (7) have demonstrated that VT was the single most important determinant of the differences between PET_{CO_2} and Pa_{CO_2}. We found no significant differences in VT or VT/FVC% between our older and younger subjects, although VT/EELV% was

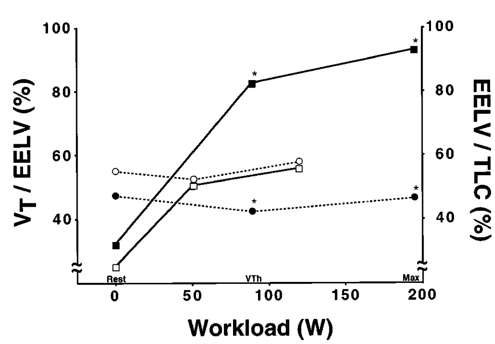

Fig. 3. Comparison of tidal volume (VT) expressed as %end-expiratory lung volume [EELV; (VT/EELV%)] and EELV expressed as %total lung capacity [(TLC); EELV/TLC%] for younger and older subjects at rest, $\dot{V}$th, and Max. □, VT/EELV% in older subjects; ■, VT/EELV% in younger subjects; ○, EELV/TLC% in older subjects; ●, EELV/TLC% in younger subjects. * Significantly different; younger compared with older subjects ($P < 0.05$).

significantly higher at $\dot{V}$th and Max for younger subjects compared with the older group. Also, in older subjects, PET_{CO_2} may not exceed Pa_{CO_2} to the same degree as occurs in younger subjects, as it has been suggested that the $PET\text{-}a_{CO_2}$ is most dependent on the VDS/VT ratio (6).

Pa_{CO_2} values have been shown to exceed PET_{CO_2} values at rest and exercise during conditions of $\dot{V}A/\dot{Q}$ inequality or increased alveolar dead space (16), both of which have been shown to increase as a consequence of aging (6, 15). Johnson et al. (6) have shown, via direct measures of Pa_{CO_2}, VDS/VT ratios in older fit individuals that were 30% higher than those of younger subjects, both at rest and during heavy exercise. VDS/VT provides a valuable estimate of the degree of matching of ventilation to perfusion in the lung during rest and exercise (16). Our data are in agreement with Johnson et al. (6), as we found significantly higher VDS/VT values for the older subjects compared with the younger at rest, $\dot{V}$th, and Max. Previously, Liu et al. (9) reported significantly lower differences between PET_{CO_2} and Pa_{CO_2} in patients with obstructive lung disease. Their data are essentially consistent with our findings, comparing differences between PET_{CO_2} and Pa_{CO_2} in both our younger and older subjects. Though direct comparisons between patients with known lung disease and our apparently normal older subjects cannot validly be made, it is tempting to speculate that a similar mechanism of $\dot{V}A/\dot{Q}$ mismatching in our older subjects contributed to the lower differences observed between PET_{CO_2} and Pa_{CO_2} compared with our younger subjects. Thus it appears that the Jones equation (7) overcorrects in situations where PET_{CO_2} does not rise to a significantly higher value than Pa_{CO_2}, as may occur under conditions of $\dot{V}A/\dot{Q}$ inequality or increased alveolar dead space. On the other hand, the differences noted between P_JCO_2 and Pa_{CO_2} at Max in our older subjects could be related to the lower CO_2 production and its influence on the slope of the PA_{CO_2} that would result in a lower PET_{CO_2} and subsequent overcorrection by the Jones equation.

From our data, we conclude that PET_{CO_2} provides the best estimate of Pa_{CO_2} at $\dot{V}$th and Max in older subjects. Both P_JCO_2 and PET_{CO_2} yield reasonable estimates of Pa_{CO_2} in older subjects at rest. However, in younger subjects, P_JCO_2 provides a reasonable estimate of Pa_{CO_2} at $\dot{V}$th but significantly underestimates Pa_{CO_2} at Max.

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