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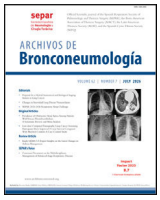

Original Article

Dynamics of Dead Space and its Components During Exercise Testing With Continuous Transcutaneous Carbon Dioxide Monitoring

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ABSTRACT

Objectives: To describe the continuous pattern of dead space during exercise and recovery using noninvasive monitoring of transcutaneous carbon dioxide pressure ($PtcCO_2$).
Methods: During routine exercise testing across various conditions in 132 subjects, including healthy individuals and patients, $PtcCO_2$ was validated against arterial sampling of carbon dioxide pressure ($PaCO_2$), and continuous dead-space recording was performed using a transcutaneous probe.
Results: During hyperventilation, a lag of 76 ± 12 s was observed between arterial and transcutaneous measurements. Comparison of $PtcCO_2$ and $PaCO_2$ values showed good accuracy, with 83% to 85% of samples within 4 mm Hg, with or without an 80-s time delay. During exercise, $PtcCO_2$ exhibited a biphasic pattern, initially increasing and then continuously decreasing beyond peak exercise during the 5-min recovery period. End-tidal carbon dioxide pressure ($PETCO_2$) was an unreliable surrogate. A decrease in dead space was observed throughout exercise, with a significant proportion occurring during the warm-up phase. The nadir occurred shortly after peak exercise, with minimum values/relative decreases ranging from 0.12/68% in healthy volunteers to 0.39/16% in patients with chronic obstructive pulmonary disease (COPD). Dead space began to increase again during the second minute of recovery, driven mainly by the mixed expired carbon dioxide fraction ($PECO_2$), and remained below resting values. The proportion of recovery ranged from 50% in healthy volunteers to 94% in patients with COPD. Dead-space dynamics were not meaningfully affected by the 80-s lag time. The $PaCO_2$–$PETCO_2$ gradient decreased to negative values for most of the test in healthy volunteers and transiently in patients.
Conclusions: $PtcCO_2$ monitoring enables continuous dead-space assessment with good accuracy. $PaCO_2$ follows a biphasic pattern independent of exercise peak and is driven by ventilation, whereas dead-space modifications closely follow exercise onset and cessation. Exercise-induced ventilatory and metabolic/vascular adjustments require more than 5 min for full recovery.

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Introduction

Exercise testing is one of the best methods for evaluating the pulmonary and circulatory systems from an integrative standpoint; the information it provides cannot be inferred from resting functional assessment. During an exercise test, numerous variables are collected, allowing computation of different indices. Among these, measurement of the dead space fraction (VD/VT) is indicative of wasted ventilation [1]. Its original computation, based on CO_2 balance, was developed by Bohr and later modified by Enghoff, who substituted arterial $PaCO_2$ for mean alveolar $PACO_2$, the accurate measurement of which is difficult. This resulted in the following formulation: $VD/VT = 1 - (863 \times VCO_2)/(PaCO_2 \times VE)$. This introduced the concept of physiological dead space, with an anatomical

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component, referring to the fraction of ventilation occurring only in the conducting airways, and an alveolar component, referring to the fraction of alveolar ventilation with absent or underperfused pulmonary circulation. This approach requires invasive sampling and is sensitive to other factors, such as ventilation–perfusion ($\dot{V}A/\dot{Q}$) heterogeneity and shunt [2,3]. Therefore, both ventilatory variables, such as VT, and mixed ventilatory-metabolic variables, such as VE/VCO_2, are important to analyze.

Because interpretation of dead-space dynamics during exercise is an important part of the diagnostic process, accurate determination of $PaCO_2$ is essential. Given the invasiveness of this measurement, the number of evaluations during the test is limited, usually to 2 or 3 snapshots at rest, peak exercise, and ventilatory threshold. However, the dynamics of dead space during exercise and recovery are not captured.

Several substitutes for $PaCO_2$ have been used, such as $PETCO_2$, the end-tidal partial pressure of CO_2 in exhaled gas. However, this is not always accurate and may overestimate or underestimate $PaCO_2$ during exercise in healthy subjects [4]. This discrepancy also occurs in patients with cardiovascular and pulmonary disease. Thus, accurate noninvasive measurement of $PaCO_2$ would be very helpful in exercise testing. $PtcCO_2$ enables measurement of PCO_2 by means of a cutaneous, noninvasive probe. However, its reliability and accuracy compared with arterial blood sampling are subject to some limitations under specific conditions. Furthermore, cutaneous $PaCO_2$ measurement exhibits a time delay relative to arterial changes (reviewed in [5]); therefore, these features require further assessment if this technique is to be used during exercise testing.

The present study was undertaken to evaluate the accuracy of $PtcCO_2$ compared with $PaCO_2$ measurement and to monitor the continuous dynamics of VD/VT during exercise and recovery in different settings, including healthy volunteers and patients.

Materials and methods

Patients were eligible if they were aged 18 years or older and were recruited during routine diagnostic cardiopulmonary exercise testing. Healthy volunteers were also recruited for exercise testing or hyperventilation. Diagnostic assignment is detailed in the supplemental files.

Approval for this study was granted by the Ethics Committee of Versailles, France. Written informed consent was obtained from all patients and volunteers. The study was registered in the NCT database under number NCT03718780.

In all cases, $PtcCO_2$ was measured with a transcutaneous probe (SenTec®, Therwil, Switzerland) clipped onto a vasodilated earlobe, with a probe temperature of 42 °C; see supplemental files. Simultaneously, $PaCO_2$ was determined by analysis of samples obtained by vasodilated earlobe puncture (arterialized blood). A few patients in intensive care were originally included for intra-arterial benchmarking; however, the low number of samples obtained ($n = 17$) precluded meaningful analysis.

The accuracy of $PtcCO_2$ measurement was evaluated by comparing paired results, arterialized blood vs transcutaneous measurements, obtained in patients or healthy volunteers during exercise testing; see supplemental files for details. In addition, healthy subjects performed voluntary 2-min hyperventilation at rest to determine the time delay between the induced arterial $PaCO_2$ modification and cutaneous recording.

Continuous dead-space measurement was performed during routine exercise testing. After a $PtcCO_2$ probe calibration/equilibration phase of 10–15 min, an incremental cycling exercise test was performed with the following steps: rest, 3 min of gentle warm-up, ramp-up with a stepwise workload increase every minute up to maximal exertion, and then 5 min of recovery. Arterialized $PaCO_2$ was sampled 4 times: at rest, at ventilatory threshold, at $\dot{V}O_{2\,peak}$, and at the end of the recovery period. $PtcCO_2$ was recorded throughout the test. Usual ventilatory and cardiac parameters were also recorded.

After completion of the exercise test, ventilatory Medisoft® data strings, generated at the various respiration-driven time points, and 1-second-interval Sentec® $PtcCO_2$ data were processed. Dead space was computed using the Bohr–Enghoff equation, based on $PECO_2$, the partial pressure of carbon dioxide in total mixed expired gas, and $PaCO_2$, with corrections for mouth tubing dead space (VD_{instr}) and $PICO_2$, the inspired partial pressure of CO_2. The following equation was used: $VD/VT = ([PaCO_2 - PECO_2]/[PaCO_2 - PICO_2]) - (VD_{instr}/VT)$. Computation was performed at each time point at which ventilatory data had been recorded, using, for $PaCO_2$ in the Bohr equation, either of the following: (a) the $PtcCO_2$ readout at the given time point, with or without consideration of the observed lag time; (b) interpolated $PaCO_2$, with interpolation performed using Expair® software and derived from the 4 earlobe samples; or (c) $PETCO_2$ measured at the given time point. For exercise data analysis and to align with arterialized $PaCO_2$ measurements, gas exchange was measured breath by breath and interpolated into 1- and 10-s average bins for all calculations, including VE/VCO_2, $PtcCO_2$, and $PETCO_2$ measurements during exercise.

The following statistical assumptions were applied; see also supplemental files. Sixty subjects were required for validation. Comparisons of PCO_2 methods were performed using Bland–Altman analysis and Passing–Bablok regression. Statistical analysis of physiological exercise variables involved groups with $n \geq 10$ and used a 2-factor mixed-effects model.

Results

Voluntary hyperventilation at rest

Voluntary hyperventilation was performed in 6 healthy volunteers. VE increased from 12.7 ± 2.3 L/min to 52.5 ± 9.4 L/min, with increases in both VT (mean +95%), and respiratory rate (RR), which tripled on average. A $PaCO_2$ nadir of 21.6 mm Hg was observed, on average, 1 min 30 s after hyperventilation onset. The mean hyperventilation duration was 1 min 58 s. $PETCO_2$ decrease mirrored the $PaCO_2$ change. An increase in VE/VCO_2 was observed. A transient increase in VO_2, mean $+27 \pm 19\%$, occurred at hyperventilation onset. VD/VT either increased slightly or remained approximately unchanged. The lag time between the observed earlobe arterialized $PaCO_2$ nadir and the recorded $PtcCO_2$ nadir was, on average, 76 ± 12 s; see Supplemental Fig. 1 and supplemental files for more details.

Comparison of $PtcCO_2$ vs $PaCO_2$

The main findings from comparisons of transcutaneous and arterial CO_2 measurements are summarized in Table 1. Results from 516 pairs during exercise tests are displayed without lag time and with either a 40- or 80-s time lag. There were very few technical failures ($n = 2$; see supplemental files). For exercise testing, the bias, defined as the mean difference between $PtcCO_2$ and $PaCO_2$, ranged from $+0.06 \pm 3$ mm Hg to -0.41 ± 3 mm Hg. Approximately 72% to 73% of $PtcCO_2$–$PaCO_2$ differences were ≤ 3 mm Hg, and 83% to 85% were ≤ 4 mm Hg, with minimal effect of time lag on these metrics and on accuracy. Fig. 1A shows the Bland–Altman analysis of $PtcCO_2$ vs $PaCO_2$, with the average difference and the 95% limits of agreement. Passing–Bablok regression (Fig. 1B) showed an intercept of 1.8 (0.00 to 3.60) and a gradient of 0.95 (0.90–1.00). These

Table 1
Summary of $PtcCO_2$ measurement performance.

Parameter	No lag time ($n = 516$)	Lag time +40 s ($n = 503$)	Lag time +80 s ($n = 456$)
Bias, mean $PtcCO_2$–$PaCO_2$ difference, mm Hg	0.06 ± 3.04	−0.25 ± 3.00	−0.41 ± 3.09
Values ≤3 mm Hg, %	72.1	73.2	71.7
Values ≤4 mm Hg, %	85.9	84.7	82.9
Accuracy, mean absolute $PtcCO_2$–$PaCO_2$ difference, mm Hg	2.31	2.27	2.37
95% limits of agreement, mm Hg	−5.90 to 6.02	−6.14 to 5.64	−6.47 to 5.64

$PaCO_2$, arterial partial pressure of carbon dioxide; $PtcCO_2$, transcutaneous partial pressure of carbon dioxide.

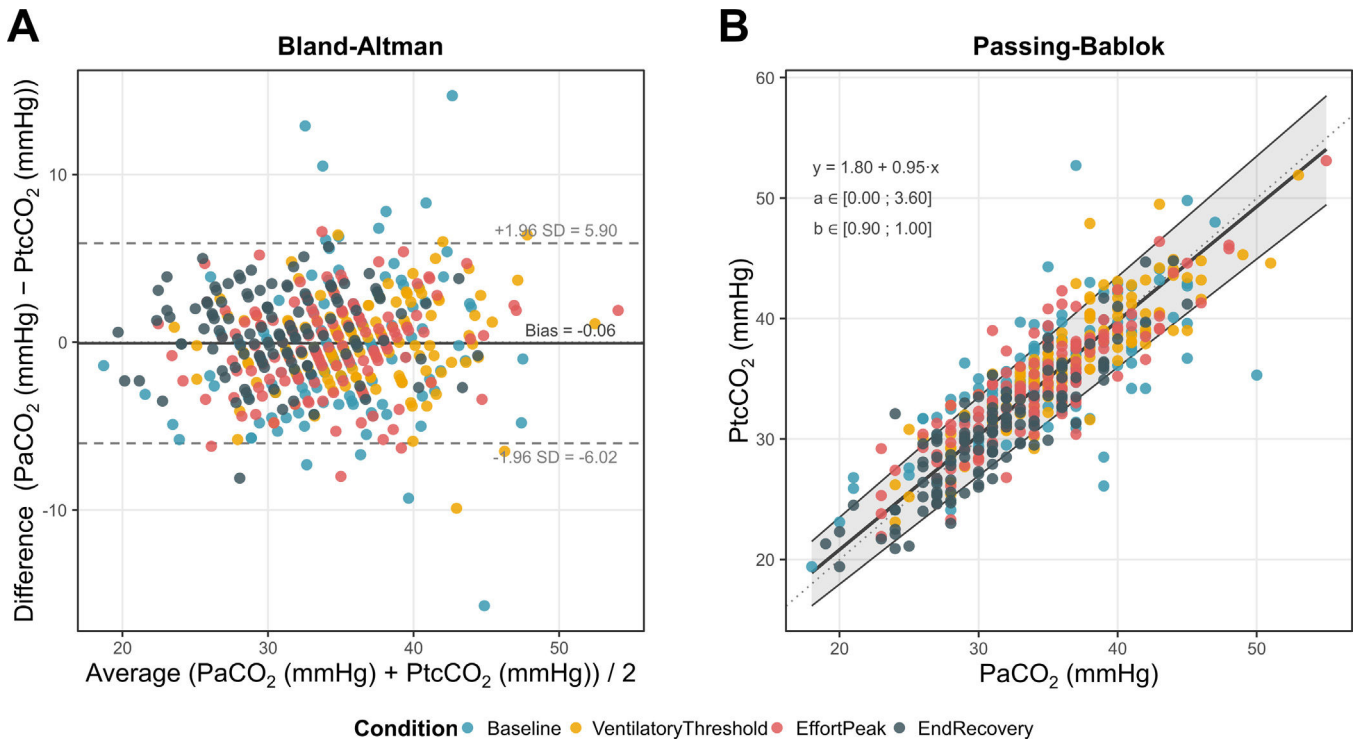


Fig. 1. Comparison of $PaCO_2$ with $PtcCO_2$. (A) Bland–Altman plots for mean $PtcCO_2$ vs $PaCO_2$. Data were obtained from patients and volunteers during exercise testing ($n = 516$ pairs). (B) Passing–Bablok regression between $PaCO_2$, measured using arterialized blood analysis, and $PtcCO_2$. Dotted lines represent the lower and upper limits of agreement; the solid line represents bias. Data points are colored according to sampling time: rest, ventilatory threshold, peak exercise, and end of recovery.

values, together with the inclusion of 0 and 1, respectively, in their confidence intervals, indicate that there was no systematic or proportional difference between the 2 methods; see also supplemental Fig. 2. $PtcCO_2$ accuracy did not vary widely across different categories of subjects or patients; see supplemental Table 1.

A total of 134 exercise tests were performed in 132 patients or subjects. The following groups were included: 32 patients with COPD, 31 with hyperventilation syndrome, 18 with heart failure, 12 healthy volunteers, 10 with asthma, 10 with interstitial pulmonary fibrosis, and 19 patients with miscellaneous diagnoses; see Table 2. Graphical display of data and statistical testing focused on the 6 main groups with $n \geq 10$. For other miscellaneous groups, see supplemental Tables 2 and 3 and supplemental Figs. 3 and 4.

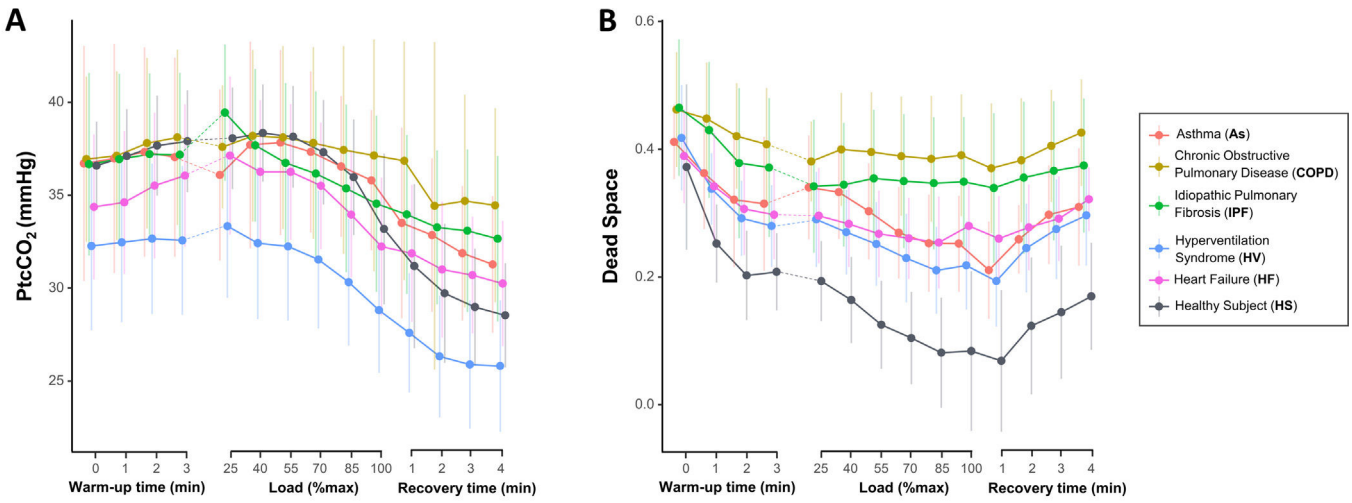
$PtcCO_2$ changes during exercise

During the exercise test, $PtcCO_2$ increased slightly during the warm-up phase and early ramp-up and then began to decrease steadily during the second part of the ramp-up until peak exercise; see Fig. 2A and supplemental Fig. 3. The slope of these changes differed significantly according to disease status, with a significant group-by-time interaction; for details, see Fig. 2A. During recovery, $PtcCO_2$ continued to decrease significantly. At the end of the 5-min recovery period, the difference between the initial pretest value and the final $PtcCO_2$ value still ranged from 2.6 mm Hg in patients with COPD to 8.7 mm Hg in patients with deconditioning; see supplemental Table 2 for full details.

Table 2
Demographic characteristics of patients and volunteers evaluated by exercise testing.

Patients/Subjects	*n*	Age, mean (SD), y	Sex, M/F
COPD	32	70 (9)	17/15
Hyperventilation syndrome	31	53 (19)	8/23
Heart failure	18	66 (9)	8/10
Asthma	11	50 (19.6)	5/6
Interstitial pulmonary fibrosis	10	64 (11)	7/3
Healthy volunteers	12	42 (11)	9/3
Miscellaneous diagnoses	**19**		
Upper respiratory tract anomaly	3	48 (5)	2/3
Pulmonary vascular disease	4	52 (27)	1/3
Sizeable muscular impairment	4	56 (8)	3/1
Deconditioning	4	61 (12)	4/0
Unexplained dyspnea	3	50 (13)	2/1

See the supplemental material for diagnostic criteria. Arterialized blood was obtained by capillary sampling, 75 µL, from a vasodilated earlobe; analysis was performed immediately using an Instrumentation Laboratory GEM 4000 arterial blood analyzer.
COPD, chronic obstructive pulmonary disease; F, female; M, male; SD, standard deviation.



A'

	Warm-up	Ramp-test	Recovery
Main effects	Time: p<0.001 Group: p<0.001 Time*Group : p=0.03	Time: p<0.001 Group: p<0.001 Time*Group : p<0.001	Time: p<0.001 Group: p<0.01 Time*Group: p=0.36
Post-hoc analysis for interaction (slope pairwise comparison)	HF vs. HV**	- COPD *vs.* HV | HF | HS*** (all) - As *vs.* HV | HF | HS*** (all)	

B'

	Warm-up	Ramp-test	Recovery
Main effects	Time: p<0.001 Group: p<0.001 Time*Group : p=0.03	Time: p<0.001 Group: p<0.001 Time*Group : p<0.001	Time: p<0.001 Group: p<0.001 Time*Group: p<0.001
Post-hoc analysis for interaction (slope pairwise comparison)	- COPD *vs.* HS**| HV* - IPF *vs.* HS | HV*(all) - HV vs. HF*	- COPD *vs.* As | HF | HS***(all) - As *vs.* IPF*** | HF* - HV *vs.* IPF | HF***(all)	- COPD *vs.* HV | HS***(all) - As *vs.* HS*

Fig. 2. Pattern of $PtcCO_2$ and dead space during exercise and recovery. Data are shown for groups with $n \geq 10$, together with statistical testing. (A) Pattern of $PtcCO_2$ measured with an 80-s lag-time correction. (A′) Associated statistics. (B) Pattern of dead space measured with an 80-s lag-time correction. (B′) Associated statistics. Data are presented successively as follows: resting value and first 3 min of warm-up, plotted on a time scale; subsequent ramp-up period of variable duration, plotted according to percentage of maximal workload achieved; and recovery period, with the same duration for all subjects, plotted on a time scale. Four minutes are represented instead of 5 because of the 80-s lag time. Both group effect and time or workload effect were significant for each phase; $p < .001$ for each. Interaction post hoc comparisons focused on pairwise slope comparisons. $p^* < .05$, $p^{**} < .01$, and $p^{***} < .001$. Comparisons not displayed were not significant, $p > .05$. Data are presented as mean ± SD.

VD/VT and its component changes during exercise

Dead space values, computed using $PtcCO_2$ with an 80-s lag-time correction, ranged at rest from 0.37 in healthy volunteers to 0.46–0.47 in patients with COPD, pulmonary artery disease, or pulmonary fibrosis (Fig. 2B and supplemental Fig. 4). In all subjects, whether patients or healthy volunteers, and in contrast to the biphasic $PaCO_2$ pattern, dead space decreased throughout the entire exercise period, with significant differences among groups with $n \geq 10$; see Fig. 2 legend and Fig. 2B′. The relative decrease in VD/VT was already substantial during the initial 3 min of gentle pedaling, ranging from 24% to 100% of the total decrease observed at peak exercise. For example, in healthy volunteers, the decrease observed at 3 min represented 54% of the decrease observed at peak exercise; see Fig. 2B and supplemental Table 3. The minimum dead space value was observed during the first minute of recovery. The absolute nadir ranged from a mean of 0.09 in healthy volunteers to 0.39 in patients with COPD, with relative decreases ranging from 16% in COPD to 76% in healthy volunteers; values in the other groups ranged between −25% and −47%; see supplemental Fig. 4 and supplemental Table 3.

The return of dead space toward resting values began during the second minute of recovery. At the end of the recovery period, dead space had not returned to its pre-exercise value. Most groups had recovered 80–94% of the resting value, whereas healthy volunteers, patients with hyperventilation syndrome, and patients with a muscular component had recovered less, ranging from 43% to 72%. Healthy volunteers had recovered only 43% of the dead-space decrease observed during exercise; see supplemental Table 3.

Patterns of the VD/VT components, VT and VE/VCO_2, are shown in Fig. 3B and D. During the rest-to-exercise transition phase, early modifications were observed, namely an increase in VT and a marked decrease in VE/VCO_2, which were maximal in healthy volunteers. At the beginning of recovery, this was mirrored by a decrease in VT and a more progressive adjustment of VE/VCO_2. At the highest workloads, 80–100%, VT often reached a plateau (Fig. 3B), and VE increased primarily through a higher respiratory rate (Fig. 3C). This may contribute to the plateau or even a small increase in VD/VT (Fig. 2B), whereas VE/VCO_2 rises mainly because of respiratory compensation for metabolic acidosis, with a minor contribution from worsening ventilation–perfusion mismatch.

Other ventilatory components and $PaCO_2$–$PETCO_2$ gradient

Changes in other ventilatory components, including $\dot{V}E$ and respiratory rate, followed the expected pattern; see Fig. 3A and C.

The $PaCO_2$–$PETCO_2$ gradient decreased from its initial resting value to a minimum observed at peak exercise and then tended to return gradually to the pretest value. In healthy volunteers, this gradient remained negative for most of exercise and recovery. Some patient groups reached a negative gradient for a limited duration during the ramp-up phase and recovery, including patients with asthma, hyperventilation syndrome, deconditioning, upper airway disease, and unexplained dyspnea (Fig. 4A). In contrast, other groups did not decrease this gradient below zero, including patients with COPD, pulmonary fibrosis, heart failure, pulmonary artery disease, and a myopathy component (Fig. 4B).

Changes in $PETCO_2$ during exercise

$PETCO_2$ levels were plotted together with $PtcCO_2$ and interpolated $PaCO_2$. Three patterns were observed: overestimation of $PaCO_2$ by $PETCO_2$, as observed in healthy volunteers (Fig. 5A); underestimation, as observed in COPD, pulmonary vascular disease, and interstitial pulmonary fibrosis (Fig. 5C); and $PETCO_2$ values close to $PaCO_2$, as observed in the other groups (Fig. 5B; see also supplemental Table 4).

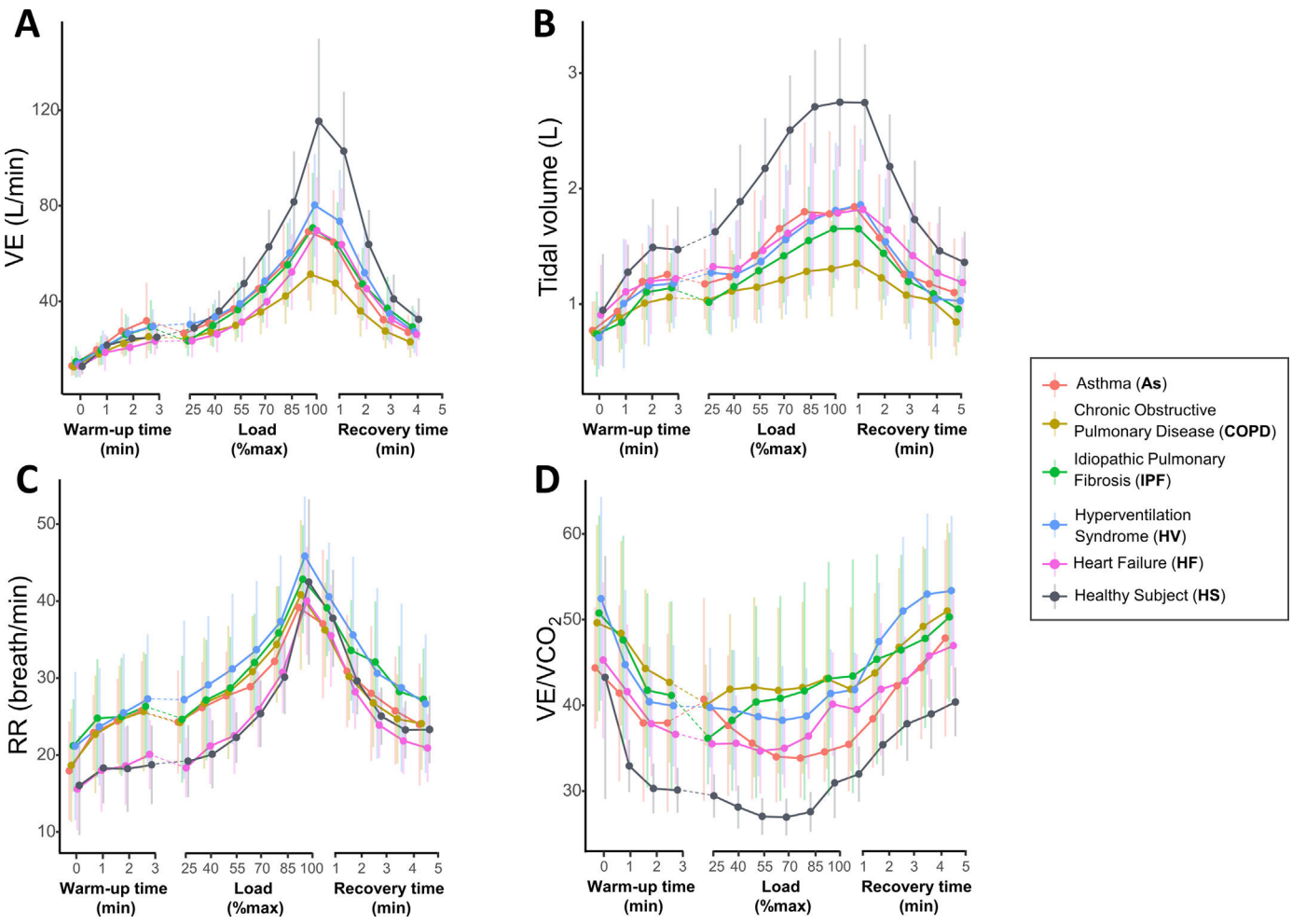


Fig. 3. Ventilatory and metabolic component patterns during exercise testing. (A), V̇E. (B) VT. (C) Respiratory rate. (D) (D) (D) VE/VCO_2. The display pattern is the same as in Fig. 2.

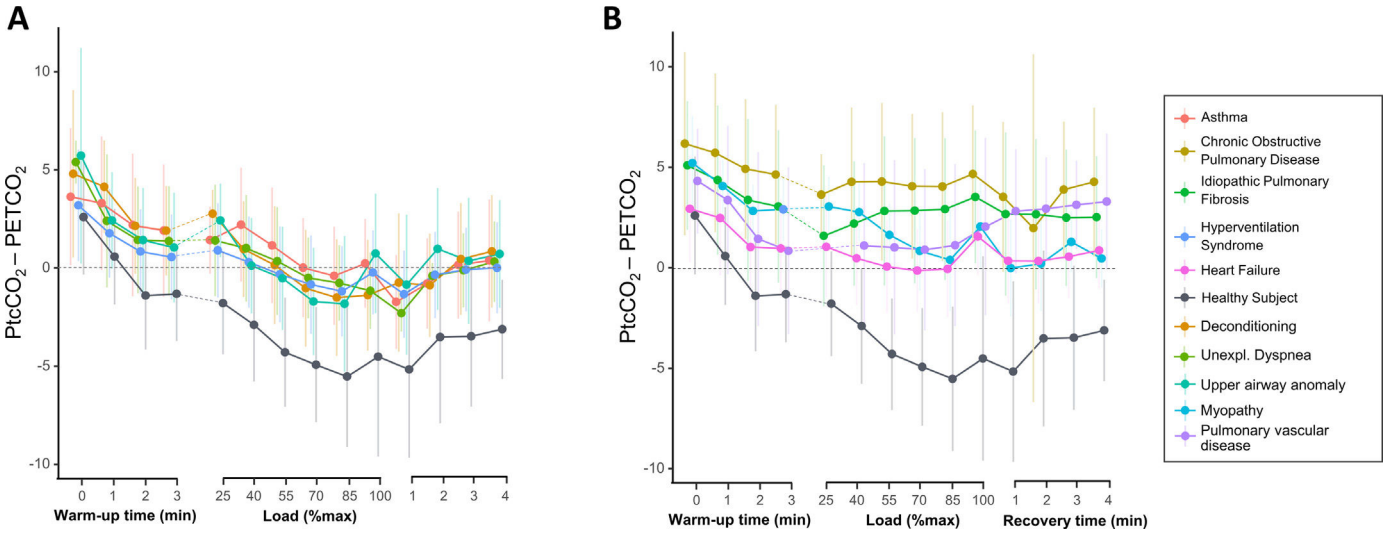


Fig. 4. Pattern of the $PtcCO_2$–$PETCO_2$ gradient during exercise. (A) Patients and subjects with a gradient decrease below zero. (B) Patients and subjects with a gradient decrease remaining above zero. Healthy volunteers are shown as the lower curve for reference.

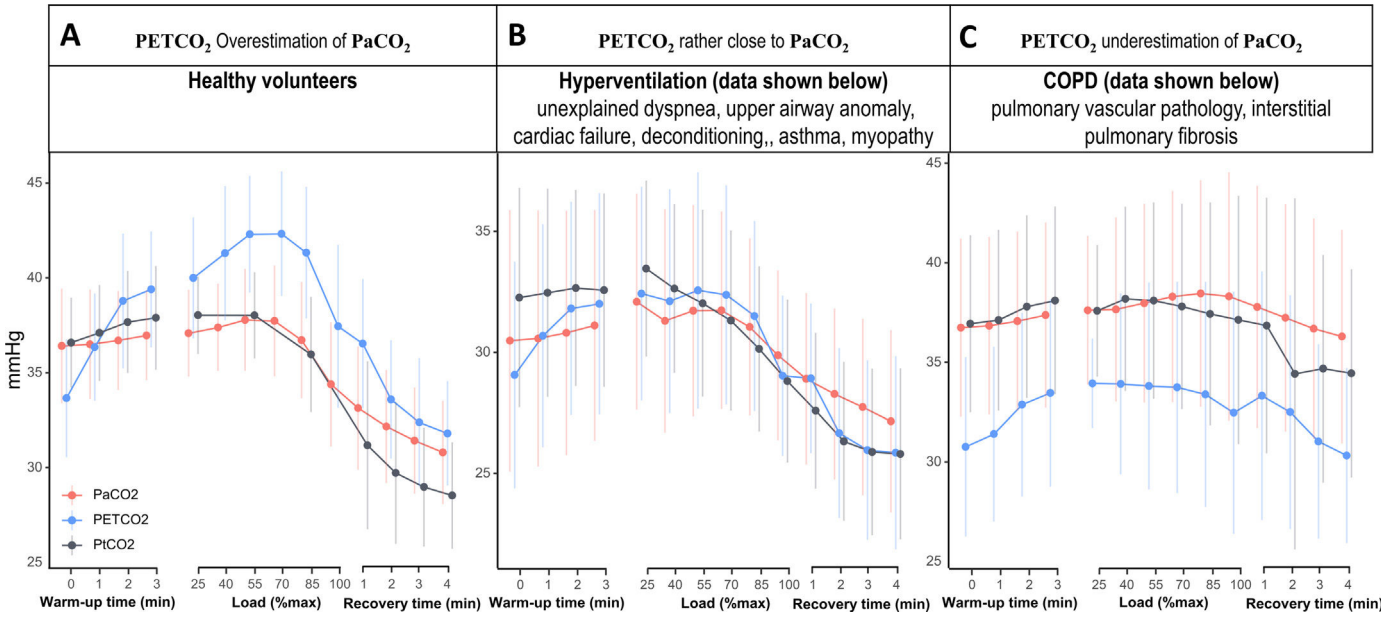


Fig. 5. Measurements of $PaCO_2$. $PaCO_2$ was determined using earlobe arterialized blood, interpolated from 4 actual values: rest, ventilatory threshold, peak exercise, and end of recovery, shown in red; continuously recorded as $PtcCO_2$, shown in black; or recorded as $PETCO_2$, shown in blue.

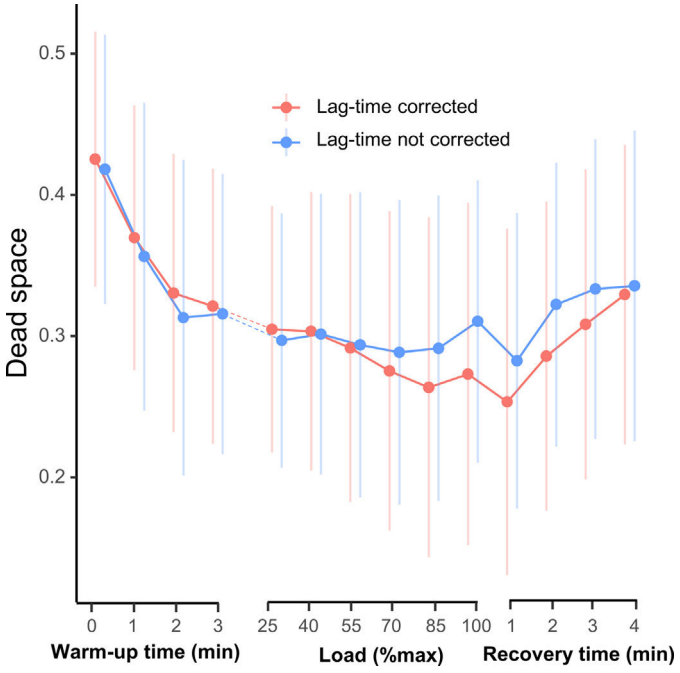


Fig. 6. Comparison of dead-space dynamics during exercise. Dead-space dynamics in all subjects and patients were computed using $PtcCO_2$ with an 80-s lag time, shown as the red curve, or without lag-time correction, shown as the blue curve.

Influence of lag time on dead-space pattern

Displaying $PtcCO_2$ values with or without the 80-s lag-time correction resulted in computed dead space values and curves that were relatively similar; see Fig. 6. Indeed, differences over the entire exercise test period were observed predominantly around peak exercise and recovery.

Discussion

To monitor the dynamics of VD/VT during exercise, we compared transcutaneous PCO_2 values with arterialized $PaCO_2$, which closely matches arterial values [6]. Our results show that the Sentec® system provides continuous and precise $PaCO_2$ readings. In our study, 72% of samples were within 3 mm Hg of $PaCO_2$, and 83% to 86% of samples were within 4 mm Hg. Bias was minimal, ranging from −0.41 to +0.06 mm Hg. This compares favorably with data from the literature. In one review [5], bias ranged from −6.1 to +3 mm Hg, and a recent study [7] reported a bias of −0.7 mm Hg, with limits of agreement between −7.8 and +6.4 mm Hg. Earlobe probe placement enables more accurate readings [8]; in addition, preliminary earlobe vasodilation may favor cutaneous gas transfer.

Transcutaneous readout introduces a time bias because of CO_2 diffusion through the skin. We showed that the total response time was approximately 80 s, as measured during a resting hyperventilation test at rest. The literature on this topic is limited; see supplemental files. Other investigators have observed values of the same order of magnitude, namely a 2-min lag time [9,10], or higher values [11], notably with differences in equipment, clinical and technical settings, and probe positioning. Although we accounted for this lag time, the observed difference did not appear to meaningfully affect clinical interpretation, as shown in Fig. 6. This is because changes in exhaled CO_2, namely $PECO_2$, have a greater impact on VD/VT during exercise transitions than gradual $PaCO_2$ shifts. However, we cannot exclude the possibility that exercise interferes with $PtcCO_2$ readings, especially around peak exercise and early recovery, as described elsewhere [12].

We observed that $PaCO_2$, after an initial slight upward trend, decreased during the second part of the exercise ramp-up and tended to overshoot during most of the recovery period. This is probably explained by persistent hyperventilation during most of recovery, as suggested by our ventilatory data during recovery; see Fig. 3A and supplemental Table 5. This is a well-known feature [13,14]. In addition, possible $\dot{V}A/\dot{Q}$ abnormalities, observed for at least 20 min after maximal exercise in healthy volunteers [15], with possible interstitial edema, may also be involved [16,17,18].

In contrast to $PaCO_2$, dead space adjusted rapidly at the very start of exercise, during the first 3 min of gentle pedaling, with a sizeable decrease ranging from 24% to 100% of the overall observed dead space decrease; see supplemental table 3. This early decrease at the beginning of very mild exercise has been described previously [19,20]. The range of maximal dead space decrease was wide,

spanning from 76% of the resting value in healthy volunteers to 16–25% of the resting value in patients with COPD or pulmonary fibrosis.

Mechanisms underlying the decrease in VD/VT include increased perfusion in the apices of the lung relative to ventilation, with improved ventilation–perfusion matching during light exercise, followed by deterioration during heavy exercise. In addition, VT increases to a much greater extent than the small increase in anatomical dead space resulting from larger airway diameter at higher ventilation [1,21,22]. This is not contradicted by the VD/VT stability observed in our *resting* hyperventilation maneuvers; indeed, besides the increase in VT, a tripling of respiratory rate was also noted. This suggests that during exercise, other factors, possibly hemodynamic, may intervene. In patients with abnormal ventilation–perfusion ratios, such as those with emphysema, cardiac disease [23], or pulmonary vascular disease [24], VD/VT is often elevated at rest and, despite a small decrease during the early phase of exercise probably related to the increase in VT, may fail to continue decreasing or may even increase as exercise progresses. Patients with COPD may also have early endothelial damage and, later, reduced pulmonary capillary volume [25].

After peak exercise, dead space began to rise again 1 min later, despite the continued downward trend in $PaCO_2$, reflecting incomplete reduction in ventilation with persistent hyperventilation. It follows from these disconnected trends that dead space reversal is driven mainly by modifications in the $PECO_2$ component of the Bohr equation, with both VT (Fig. 3B) and VE/VCO_2 (Fig. 3D) initiating a progressive return toward resting values. The speed and extent of recovery depend both on the magnitude of the changes induced by the exercise challenge, with deeper adaptive changes requiring longer readjustment, and on the adaptability of the pulmonary microvasculature according to etiology. Some patient groups, including COPD and deconditioning, almost recovered their resting dead space value at the 5-min recovery mark. In the other groups, as in healthy volunteers, dead space had not returned to pretest values. Our data show that many of the changes, especially ventilation, were not fully reversed by the end of 5 min. The presumed persistence of postexercise $\dot{V}A/\dot{Q}$ abnormalities in healthy volunteers may also apply to patients. Additional mechanisms may also be involved in some groups. For example, groups with sizeable hyperventilation may have a persistent abnormal ventilatory pattern independent of the pulmonary $\dot{V}A/\dot{Q}$ ratio.

This study confirms that noninvasive $PETCO_2$ is not an adequate substitute for $PaCO_2$ measurement. Bias ranged from underestimation of $PaCO_2$ to overestimation, particularly in healthy volunteers, with a gray zone for some patient groups. Conversely, $PtcCO_2$ appears to be a good surrogate for $PaCO_2$, enabling accurate monitoring of dead space dynamics. However, when comparing dead space data computed with $PtcCO_2$ with those obtained using interpolated values from 4 discrete $PaCO_2$ samples obtained during the test, namely at rest, ventilatory threshold, peak exercise, and the end of recovery, the added value appears marginal because the slow variation in $PaCO_2$ over time makes interpolation reasonably accurate. However, this holds true only when 4 arterial $PaCO_2$ values are sampled throughout the exercise test, including at the end of recovery, which is almost never the case. Nevertheless, continuous transcutaneous measurement can substitute for invasive and potentially painful arterial sampling.

Weaknesses of our study include the limited number of patients in some groups. Although the COPD, hyperventilation syndrome, heart failure, healthy volunteer, and asthma groups were sizeable, other groups were small, with $n = 3–4$ each. This precludes any strong group-specific conclusion for these latter groups. However, no unexpected finding singled out any of these small groups, and, aside from nuances, the main findings were shared across all groups.

Conclusions

In summary, continuous $PtcCO_2$ monitoring during exercise testing is feasible and accurate, unlike $PETCO_2$, and enables dynamic dead-space computation. Transcutaneous lag time does not meaningfully affect the VD/VT pattern. In all tested patients and subjects, $PaCO_2$ decreased significantly during exercise and beyond, most often without returning to baseline values, driven by persistent hyperventilation. In contrast, dead space began to adjust immediately at exercise onset, even at low intensity, and began readjusting early after exercise cessation, also without returning to pretest values. The magnitude of dead-space adjustments ranged from those observed in healthy volunteers at one end of the spectrum to those observed in patients with COPD at the other, without any particular differentiating feature among the various patient groups. Ventilatory, vascular, and metabolic adjustments induced by maximal exercise require more than 5 min for full reversal.

Authors' contributions

Serge Kouzan: conceptualization, investigation, methodology, project administration, resources, supervision, validation, writing – original draft, and writing – review and editing. Léo Blervaque: conceptualization, data curation, formal analysis, methodology, resources, software, visualization, and writing – review and editing. Vincent Peigne: conceptualization, investigation, methodology, resources, validation, and writing – review and editing. Cécile Ricard: data curation, formal analysis, methodology, resources, software, validation, visualization, and writing – review and editing. Fabienne Prieur: data curation, investigation, project administration, resources, and writing – review and editing. Pierantonio Laveneziana: conceptualization, methodology, supervision, validation, visualization, and writing – review and editing.

Artificial intelligence

The authors declare that no artificial intelligence program or tool was used in the writing of this article or in the production of tables, figures, legends, or references.

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Conflicts of interest

PL reports personal fees and support for attending meetings and/or travel from Chiesi, Trudell International, and Elivie, outside the submitted work. SK, LB, VP, CR, and FB report no competing interests.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.arbres.2026.06.017.

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