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Are Transcutaneous O₂ and CO₂ determinations of value in Pulmonary Arterial Hypertension?

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Abstract

Background—We hypothesized that transcutaneous gas determinations of O₂ and CO₂ (TcPO₂ and TcPCO₂) are associated with the severity of pulmonary arterial hypertension (PAH).

Methods—In this cross-sectional study we included consecutive patients with PAH (group 1 pulmonary hypertension (PH)) (n=34). Transcutaneous gas determinations were compared to those of age- and gender-matched healthy controls (n=14), non-group 1 PH (n=19) or patients with high estimated right ventricular systolic pressure on echocardiography but without hemodynamic evidence of PH (n=12).

Results—In patients with PAH, TcPO₂ and TcPCO₂ were significantly associated with PaO₂ (R= 0.44, p=0.03) and PaCO₂ (R=0.77, p<0.001), respectively. TcPO₂/FiO₂ (mean difference: -65.0 [95% CI: -121.3–8.7]) and TcPCO₂ (mean difference: -7.4 [95% CI: -11.6–3.1]) were significantly lower in patients with PAH than healthy controls. TcPCO₂ was useful in discriminating PAH patients from other individuals (AUC: 0.74 (95% CI of 0.62–0.83)). TcPO₂/FiO₂ ratio was significantly associated with mean PAP, TPG, PVR, CI, SVI, DLCO, 6-min walk distance and components of the CAMPHOR questionnaire.

Conclusions—Transcutaneous pressure of CO₂ was lower in patients with PAH. Transcutaneous pressure of O₂ over inspired fraction of O₂ ratio was inversely associated with severity of disease in patients with pulmonary arterial hypertension.

Keywords

Pulmonary arterial hypertension; arterial blood gases; oxygen; carbon dioxide; transcutaneous oxygenation; microcirculation; vascular function

Introduction

Pulmonary Arterial Hypertension (PAH) is a pulmonary vascular disease that despite remarkable therapeutic advances in the last two decades, continues to be responsible for right ventricle failure and premature death [28]. There is a pressing need to identify methods that allow a comprehensive non-invasive assessment of this life-threatening condition.

Previous guidelines included arterial blood gas (ABG) analysis as part of the evaluation of patients with pulmonary hypertension (PH) [10,17]. This was in part supported by a retrospective study that identified lower partial pressure of carbon dioxide (CO₂) (measured in arterialized capillary blood obtained from hyperemic earlobes) as an independent predictor of mortality in patients with idiopathic PAH [13]. The recently published, Fifth World Symposium on PH still suggests considering ABG analysis in the diagnostic work-up of patients with PH [12].

Arterial blood gas analysis is not routinely done in the diagnostic evaluation of patients with PAH, mostly due to its invasive nature. In order to avoid the arterial puncture, several authors have proposed the measurement of blood gases in arterialized capillary blood (hyperemic earlobes) or the determination of CO₂ at the end of expiration (EtCO₂); nevertheless, these methodologies have limitations [5,18,22,25]. An alternative non-invasive approach is the measurement of the transcutaneous PO₂ and PCO₂ (TcPO₂ and TcPCO₂,

respectively) by a locally applied skin electrode that reflected the amount of O₂ and CO₂ that diffuses from the capillaries through the skin into the sensors. Transcutaneous gas determinations are affected by respiratory or circulatory conditions that influence the delivery of O₂ or extraction of CO₂ [20]. TcPO₂ provides a direct and quantitative assessment of the O₂ availability to the tissues and is commonly used in medical decision making in wound care and hyperbaric medicine [20].

We hypothesized that transcutaneous gas determinations would approximate the values obtained with ABG analysis and that these non-invasive measurements are associated with the severity of PAH. Therefore, in the present study we tested how transcutaneous gas measurements (TcPO₂ and TcPCO₂) compare to ABG analysis and their association with functional, laboratory, echocardiographic and hemodynamic parameters in patients who underwent RHC at our institution. Our cohort of interest was patients with PAH (5th World Symposium group 1 PH) [26]. Given the difficulties in finding a valid comparator, we studied 3 other groups of subjects: non-group 1 PH [26], patients without PH on RHC who were studied because of a high right ventricular systolic pressure (RVSP) on echocardiogram and age- and gender-matched healthy controls. Preliminary results of this study have been previously reported in the form of an abstract [3].

Methods

a) Subjects and study design

The research protocol was approved by the Cleveland Clinic Institutional Review Board (study # 11-441) and all subjects provided written informed consent. We conducted this cross-sectional study between December 2011 and December 2013. We included consecutive patients that met hemodynamic criteria for PAH (defined as mean PAP ≥ 25 mm Hg, PAWP ≥ 15 mm Hg and PVR > 3 Wood Units) [12]. In addition, we studied patients with non-group 1 PH [26] and patients that underwent a RHC due to a high RVSP on echocardiogram and were subsequently found to have a mean PAP < 25 mmHg. A detailed clinical evaluation was performed in all patients to determine the etiology of PH [12]. In addition, we tested age- and gender-matched healthy controls. Healthy controls did not have ABG analysis, echocardiograms or RHC.

Patients underwent RHC in the outpatient setting using local anesthesia (lidocaine 2%) and cannulating preferably the right internal jugular vein. No intravenous sedation or analgesia was given to any patient before, during or after the procedure. Patients did not eat or drink for 8 hours prior to testing. We continued or started O₂ supplementation in patients on chronic O₂ therapy or in whom the pulse oxygen saturation (SpO₂) was below 90%, respectively. In the event that O₂ supplementation was provided to the patients, we maintained the same O₂ flow during all the study measurements. The procedure room had stable temperature (72° F or 22° C) during all the interventions.

During the RHC, we obtained mixed venous O₂ from the pulmonary artery. Immediately after the RHC, we obtained radial ABG and determined forearm TcPO₂ and TcPCO₂. Furthermore, we measured the EtCO₂ and partial pressure of expired CO₂ (PeCO₂) and calculated the alveolar dead space (Figure 1). Given that the metabolic cart determinations

were incorporated after the initiation of the study, EtCO₂ and PeCO₂ were measured in only 29 patients who underwent RHC. Meanwhile, ABGs were not done in 5 patients (2 patients declined the procedure and in 3 patients the procedure was aborted given that arterial blood was not obtained after 2 attempts).

b) ABG analysis, PeCO₂ and EtCO₂ determinations

Brachial, radial and ulnar pulses were of good quality and none of the patients had known peripheral vascular disease. Arterial blood was obtained from the radial artery and analyzed in the ABL 800 Flex analyzer (Radiometer, Copenhagen, Denmark). This instrument uses 128 wavelengths for full CO-oximetry which allowed the precise measurement of the relative blood concentrations of oxyhemoglobin (SaO₂).

EtCO₂, PeCO₂ and tidal volume (V_t) were determined using the CCM Express indirect calorimeter (MGC diagnostics, Saint Paul, Minnesota). During the course of 15 minutes, the EtCO₂ and PeCO₂ were determined breath by breath and the 30-second means were averaged. We calculated the physiological dead space (V_d): $(\text{PaCO}_2 - \text{PeCO}_2) / \text{PaCO}_2 * V_t$ - face mask dead space [2,6,27].

c) TcPO₂ and TcPCO₂ determinations

We used the PeriFlux system 5000 (Perimed, Järfälla, Sweden) that included the PF 5040 TcPO₂/TcPCO₂ unit and the E5280 electrode. This electrode is covered with a thin membrane that stabilizes the conditions and is permeable to O₂ and CO₂. Per manufacture's protocol, the electrode warms the underlying tissue (45°C) to achieve greater skin gas diffusion. TcPO₂ is determined by direct polarography, based on an electro-chemical process that involves a platinum cathode (sensor electrode) and a silver anode (reference electrode). The reduction of O₂ at the cathode generates a current which is later converted into voltage and digitalized. TcPCO₂ is electrochemically calculated by a change in PH of an electrolyte solution [20].

For transcutaneous gas determinations, patients were in a sitting position with the right forearm at the level of the heart (Figure 1). The membrane of the E5280 transcutaneous electrode was changed weekly following the manufacturer's recommendations. The transcutaneous electrode was calibrated before each measurement. The electrode was applied in the anterior aspect of the right forearm away from blood vessels and 5 cm distal to the antecubital fossa. We chose the forearm because this site is easily accessible and commonly used for studies of microvascular function.

The skin of the forearm was prepared by applying a clean adhesive tape that removes part of the stratum corneum. After wiping the area with alcohol, a TC 550 fixation ring was applied to the skin and 3 to 5 drops of contact liquid (TC 560) we instilled before mounting the electrode. The TcPO₂ and TcPCO₂ measurements were obtained by two operators (L.A., F.C.) immediately after the RHC. Transcutaneous gas readings were recorded and analyzed off-line. We measured TcPO₂ and TcPCO₂ after at least 20 minutes of the application of the electrode and once values stabilized. Operators were blinded to the hemodynamic determinations or severity of the clinical condition.

d) Functional, echocardiographic and hemodynamic measurements

We determined the severity of PAH by using NYHA (New York Heart Association) functional class, plasma NT-pro brain natriuretic peptide (NT-pro BNP) concentration, diffusing capacity of carbon monoxide (DLCO) by single-breath technique [15], distance walked in the 6-minute [1] and right ventricular (RV) size and function on echocardiography [23]. RV function was determined by the tricuspid annular plane systolic excursion (TAPSE); meanwhile, RV size was measured in the apical four-chamber view by the RV basal, middle cavity and longitudinal dimensions [23]. We assessed quality of life with the Cambridge Pulmonary Hypertension Outcome Review (CAMPHOR) questionnaire [16]. We measured and calculated the following hemodynamic parameters during RHC: right atrial pressure, mean pulmonary artery pressure (PAP), pulmonary artery wedge pressure (PAWP), transpulmonary gradient (TPG: mean PAP - PAWP), diastolic pulmonary gradient (DPG: diastolic PAP - PAWP), cardiac index (CI), stroke volume index (SVI) and pulmonary artery vascular resistance (PVR).

Statistical analysis

Continuous data are presented as mean $\pm$ standard deviation (SD) and categorical data are summarized as discrete values and percentages (n (%)). Independent continuous samples were compared using Kruskal Wallis one-way analysis of variance by ranks and the post hoc Games-Howell test for pairwise comparison. Categorical variables were compared with Fisher's exact test. Relationships between parameters were tested using the Pearson correlation test. Agreement was tested with Bland-Altman plot and expressed as mean difference and limit of agreement (LOA). Receiver Operating Characteristic (ROC) curves were constructed and values provided as area under the curve (AUC) with their respective 95% confidence interval. Given that some patients were on O₂ supplementation, we performed the TcPO₂ analyses on the entire cohort using the calculated TcPO₂/FiO₂ ratio and additionally only in the subgroup of patients not on O₂ therapy. All *p* values are two-tailed and a value of < 0.05 was considered significant. The statistical analyses were performed using the statistical package IBM SPSS, version 20 (IBM; Armonk, New York) and MedCalc, version 13 (Ostend, Belgium).

Results

a) Patient characteristics

We included 34 patients with group 1 PAH (idiopathic or heritable: 18 (53%), connective tissue disease associated: 7 (21%), porto-pulmonary hypertension: 6 (18%), congenital heart disease: 2 (6%) and due to human immunodeficiency virus: 1 (3%)). Of the patients with PAH, 24 (71%) were receiving PH-specific treatment (only oral treatment: 15 (63%), parenteral or inhaled prostacyclin analogues: 9 (37%)).

We also included, 14 patients with non-group 1 PH (5th World Symposium groups II: 5 (36%), III: 3 (21%), IV: 4 (29%), and V: 2 (14%)), 11 patients with elevated right ventricular systolic pressure (> 40 mm Hg) on echocardiogram but no PH on RHC, and 14 healthy controls. The clinical, functional, echocardiographic and hemodynamic characteristics of the study subjects are presented in Table 1.

Measurements of transcutaneous gases, ABGs and EtCO₂ are presented in Table 2 for the entire cohort and for those patients not on O₂ supplementation. In the entire cohort of patients TcPO₂/FiO₂ (mean difference: -65.0 [95% CI: -121.3–8.7]) and TcPCO₂ (mean difference: -7.4 [95% CI: -11.6–3.1]) were significantly lower in patients with PAH than healthy controls. Interestingly TcPCO₂ was significantly lower in patients with PAH compared to other PH groups (mean difference: -7.1 [95% CI: -14.0–0.2]). Treatment for PAH did not significantly affected any of the O₂ or CO₂ measurements (data not shown).

b) Difference and agreement between transcutaneous gases and ABGs

Using Bland-Altman analysis the mean difference between TcPO₂ and PaO₂ was -2 mmHg with wide 95% LOA (25 mmHg to -29 mmHg). In patients not on O₂ supplementation the Bland-Altman analysis showed a mean difference between TcPO₂ and PaO₂ of -0.2 mmHg with 95% LOA of 19.4 mmHg to -19.7 mmHg. In patients that underwent RHC the same analysis revealed a mean difference between TcPCO₂ and PaCO₂ of -3.1 mmHg with 95% LOA of 8.8 mmHg to -15 mmHg.

c) Associations between TcPO₂/FiO₂ ratio and TcPCO₂ versus functional, laboratory, echocardiographic and hemodynamic parameters in PAH patients

In the entire cohort of PAH patients TcPO₂/FiO₂ ratio was significantly associated with TPG, PVR, CI and SVI as well as the activities and QOL components of the CAMPHOR questionnaire and DLCO (Table 3). When only considering the PAH patients not on O₂ supplementation, TcPO₂ was inversely associated with TPG and the activities and QOL components of the CAMPHOR questionnaire. TcPCO₂ was indirectly associated with TPG and the activities and QOL components of the CAMPHOR questionnaire; meanwhile other associations did not reach statistical significance.

d) TcPCO₂ as a predictor of PAH and TcPO₂/FiO₂ ratio as a predictor of severity of disease in PAH

We used ROC test to assess whether TcPCO₂ could help differentiate patients with PAH from individuals with non-group 1 PH and those with normal pulmonary pressure in RHC. The area under the ROC curve (AUC) was 0.74 (95% CI of 0.62–0.83) and a TcPCO₂ cut-off of 34.4 mmHg had a sensitivity and specificity of 79% and 74%, respectively to predict PAH, with a positive likelihood ratio of 2.99 (95% CI: 1.7–5.2). Meanwhile, a TcPCO₂ cut-off of 32.2 mmHg had a sensitivity and specificity of 64% and 84%, respectively, with a positive likelihood ratio of 4.0 (95% CI: 1.9–8.8) (Figure 2, Panel A).

We tested whether TcPO₂/FiO₂ could help identify PAH patients who were not on supplemental O₂ and had more severe hemodynamic profile defined as a PVR below or above the median. The AUC was 0.72 (95% CI: 0.52–0.86) and a cut-off value of 274 mmHg had a sensitivity of 46% and specificity of 100% to discriminate between patient with PVR 7.5 Wood Units (Figure 2, Panel B).

Discussion

Since the publication of the National Institute of Health (NIH) national registry it is known that PAH is associated with mild to moderate hypoxemia and hypocapnia [21]. Limited information is available to determine the degree in which this ABG pattern reflects disease severity and how it relates to non-invasive determinations. For the first time, we have tested transcutaneous gas measurements in patients with PH and compared them with arterial gas determinations as well as several other important clinical parameters. Overall, we found that O_2 and CO_2 transcutaneous gas determinations are of value in PAH since a lower $TcPO_2/FiO_2$ ratio was associated with severity of disease and $TcPCO_2$ may help with the identification of PAH patients.

Transcutaneous monitoring has no absolute contraindications and it is non-invasive. A decrease in the peripheral perfusion or capillary density may result in a decrease in $TcPO_2$ and $TcPCO_2$; hence these measurements can be used to determine the adequacy of tissue perfusion [9,20]. We tested this noninvasive methodology in patients with PAH, a condition that with time leads to decrease cardiac output and poor peripheral perfusion. In addition, there is mounting evidence that PAH is not only a disease limited to pulmonary vasculature but also affects the systemic microcirculation [4,14]. Hofstee et al. found that a reduction in nailfold capillary density was associated with PAH severity in patients with systemic sclerosis or idiopathic PAH[14]. Further investigations are needed to determine whether the lower $TcPO_2/FiO_2$ ratio noted in our study is a reflection of a decrease cutaneous capillary density, particularly in patients with more severe PAH.

As noted by previous investigations, transcutaneous gas determinations showed a very good association between $TcPCO_2$ and $PaCO_2$ [11,24] and a weaker association between $TcPO_2$ and PaO_2 . Hence, $TcPCO_2$ could adequately estimate $PaCO_2$ in clinical practice; however, given the large limits of agreement between the measurements the same does not hold true for $TcPO_2$ and PaO_2 .

A retrospective analysis by Hoeper et al. showed that a lower PCO_2 in arterialized capillary blood gases was a strong and independent predictor of survival in patients with idiopathic PAH [13]. In addition, lower $EtCO_2$ values have been reported in PAH [29,30]. These findings are likely due to ventilatory inefficiency in PAH which is attributable to an increase in dead space fraction and sensitivity of chemoreceptors together with a decrease in cardiac output [8,13,19]. In our study, $TcPCO_2$ does not appear to be related to variables that predict prognosis in PAH. Nevertheless, we found that $TcPCO_2$ was lower in PAH patients than in other groups of patients. In support of our findings, prior investigations showed a lower $PaCO_2$ in PAH patients [13].

Hoeper et al. showed an inverse association between arterialized capillary PO_2 and RA pressure but no association with mean PAP or PVR [13]. Our study found a significant association between the ratio of $TcPO_2/FiO_2$ and several parameters that track with disease severity. In PAH patients not on supplemental O_2 , $TcPO_2$ was associated with TPG and CAMPHOR questionnaire scores. Some associations between parameters of disease severity

and TcO_2 were noted only for $\text{TcPO}_2/\text{FiO}_2$ and not for TcPO_2 , potentially due to the smaller sample size when PAH patient on supplemental O_2 are excluded.

There are limitations in this exploratory analysis that tested invasive and non-invasive methodologies that measure O_2 and CO_2 tension at different levels in patients that underwent RHC due to the suspicion of PH. Firstly, our sample size is relatively small; however PAH is a rare disease and despite working in a large academic center it took us 2 years to collect data on the patients presented in this study. Secondly, for a variety of reasons not all gas measurements were performed in all patients. Thirdly, we did not obtain arterialized capillary blood and healthy controls did not have an echocardiogram or blood work as part of the study. The strengths of this investigation are that ABG and novel gas measurements were performed immediately after the right heart catheterization which is the gold standard for diagnosing the disease and a critical tool for assessing severity of disease.

Conclusions

A lower transcutaneous pressure of CO_2 suggested the presence of pulmonary arterial hypertension. In patients with pulmonary arterial hypertension, a lower ratio of transcutaneous pressure of O_2 over the inspired fraction of O_2 was associated with a worse pulmonary hemodynamic profile.

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Abbreviations

ABG	arterial blood gas
CAMPHOR	Cambridge Pulmonary Hypertension Outcome Review
CO_2	carbon dioxide
EtCO_2	end-tidal carbon dioxide
FiO_2	fraction of inspired oxygen
NT-pro BNP	NT-pro brain natriuretic peptide
NYHA	New York Heart Association
O_2	oxygen
PAH	pulmonary arterial hypertension
PaCO_2	partial pressure of carbon dioxide in arterial blood
PAWP	pulmonary artery wedge pressure
PaO_2	partial pressure of oxygen in arterial blood

PAP	pulmonary artery pressure
PeCO₂	partial pressure of expired CO ₂
PH	pulmonary hypertension
PVR	pulmonary artery vascular resistance
RHC	right heart catheterization
RV	right ventricle
SpO₂	pulse oxygen saturation
TAPSE	tricuspid annular plane systolic excursion
TcPCO₂	transcutaneous partial pressure of carbon dioxide
TcPO₂	transcutaneous partial pressure of oxygen
TPG	transpulmonary gradient
Vd	physiological dead space
Vt	tidal volume

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Figure 1. Measurements performed

Upper panel: To the left of the subject we observed the CCM Express indirect calorimeter (MGC diagnostics, Saint Paul, Minnesota) and the PeriFlux system 5000 (Perimed, Järfälla, Sweden). To the right of the subject we can see the transcutaneous electrode (E5280) in the anterior aspect of the right forearm and an arterial blood collection kit. Lower panel: TcPO₂ and TcPCO₂ measurements. The arrows point to the recorded values for this particular patient.

Figure 2. ROC curves for TcPCO₂ and TcPO₂/FiO₂

Panel A shows the ROC curve of TcPCO₂ for discriminating patients with PAH from the cohort of subjects that underwent RHC. Panel B depicts that ROC curve of TcPO₂/FiO₂ for discriminating patients with a PVR above the median (7.5 Wood Units).

Table 1

Characteristics of the study subjects:

	PAH (Group 1 PH) Mean $\pm$ SD, median (range) or n (%)	Non-group 1 PH Mean $\pm$ SD, median (range) or n (%)	No PH on RHC Mean $\pm$ SD, median (range) or n (%)	Healthy controls Mean $\pm$ SD or n (%)	P (Kruskal Wallis/ Fisher's exact test)
n	34	14	11	14	
Age (years)	54 $\pm$ 13	58 $\pm$ 13	56 $\pm$ 17	51 $\pm$ 11	0.59
Female gender	27 (79)	8 (57)	5 (46)	11 (79)	0.12
BMI (kg/m²)	29.4 $\pm$ 6	32.1 $\pm$ 7	28.8 $\pm$ 13	-	0.60
Patients on O₂ supplementation[#]	9 (27)	3 (21)	0 (0)	0 (0)	0.04
6-min walk distance (% of predicted)[7]	64 $\pm$ 21	58 $\pm$ 18	72 $\pm$ 22	-	0.40
NT-pro BNP (pg/mL)	1888 $\pm$ 2053	1753 $\pm$ 2162	96 $\pm$ 50	-	0.01
DLCO (% of predicted)	59 $\pm$ 21	54 $\pm$ 23	70 $\pm$ 18	-	0.30
CAMPBOR (symptoms)	12.7 $\pm$ 6	9.9 $\pm$ 7	3.8 $\pm$ 3	-	0.03
CAMPBOR (activity)	11.7 $\pm$ 7	7 $\pm$ 4	3.8 $\pm$ 4	-	0.03
CAMPBOR (QOL)	9.7 $\pm$ 7	7 $\pm$ 7	3.2 $\pm$ 3	-	0.12
TAPSE (cm)	1.8 $\pm$ 0.6	1.8 $\pm$ 0.8	2.11 $\pm$ 0.4	-	0.27
Basal RV diameter (cm)	4.3 $\pm$ 0.7	4.5 $\pm$ 0.6	4.7 $\pm$ 0.8	-	0.32
Mid RV diameter (cm)	4.0 $\pm$ 1.1	4.0 $\pm$ 0.8	3.6 $\pm$ 1.0	-	0.70
Longitudinal RV diameter (cm)	6.8 $\pm$ 1.1	7.0 $\pm$ 1.2	7.0 $\pm$ 1.4	-	0.54
Heart rate (bpm)	77 $\pm$ 11	79 $\pm$ 20	70 $\pm$ 17	-	0.19
Systolic ABP (mmHg)	121 $\pm$ 29	138 $\pm$ 25	127 $\pm$ 18	-	0.10
RA pressure (mmHg)	8 $\pm$ 5	11 $\pm$ 8	6 $\pm$ 3	-	0.04
Mean PAP (mmHg)	46 (25.0–73.0)	38.5 (25.0–60.0)	20.0 (18.0–23.3)	-	<0.001
PAWP (mmHg)	11 $\pm$ 6	15 $\pm$ 6	12 $\pm$ 3	-	0.03
CI (L/min/m²)	3.0 $\pm$ 1.2	3.0 $\pm$ 0.7	2.9 $\pm$ 0.7	-	0.87
SVI (ml/m²)	41 $\pm$ 15	39 $\pm$ 10	43 $\pm$ 8	-	0.58
PVR (Wood units)	7.5 (3–16)	4.0 (0.1–8)	1.7 (1–7)	-	<0.001
Mixed venous O₂ (%)[*]	68 $\pm$ 8	66 $\pm$ 10	69 $\pm$ 7	-	0.69
Lactic acid in arterial blood (mmol/L)	1.0 $\pm$ 0.4	1.0 $\pm$ 0.5	1.0 $\pm$ 0.3	-	0.41

Abbreviations: ABP: arterial blood pressure, BMI: body mass index, CI: cardiac index, DLCO: diffusing capacity of carbon monoxide, FiO₂: fraction of inspired O₂, NT-pro BNP: N-terminal pro-brain natriuretic peptide, PAH: pulmonary arterial hypertension, PAWP: pulmonary artery wedge pressure, PAP: pulmonary artery pressure, PH: pulmonary hypertension, PVR: pulmonary vascular resistance, QOL: quality of life, RA: right atrial, RV: right ventricle, SD: standard deviation, SVI: stroke volume index, TAPSE: tricuspid annular plane systolic excursion.

* on patients not on oxygen supplementation.

in patients on O₂ supplementation the flow (L/min) was 3.6 ± 1 and 4.0 ± 1 for PAH and non-group 1 PH patients, respectively.

Table 2

Comparison of ABGs, transcutaneous and EtCO₂ in the study subjects.

	PAH (Group 1 PH) Mean $\pm$ SD or n (%)	Non-group 1 PH Mean $\pm$ SD or n (%)	No PH on RHC Mean $\pm$ SD or n (%)	Healthy controls Mean $\pm$ SD or n (%)	P (Kruskal-Wallis/Fisher's exact test)
Measurements on all patients					
n	34	14	11	14	
TcPO₂/FIO₂ ratio (mmHg)	338 $\pm$ 69	324 $\pm$ 69	393 $\pm$ 59	403 $\pm$ 58	0.005
PaO₂/FIO₂ ratio (mmHg)	342 $\pm$ 81	328 $\pm$ 99	375 $\pm$ 47	-	0.40
TcPCO₂ (mmHg)	31.6 $\pm$ 7	37.8 $\pm$ 7	33.4 $\pm$ 10	38.9 $\pm$ 3	0.001
PaCO₂ (mmHg)	33 $\pm$ 5	40.7 $\pm$ 5	42 $\pm$ 4	-	<0.001
PaCO₂ - TcPCO₂ (mmHg)	1.9 $\pm$ 4.9	3.1 $\pm$ 3.9	5.1 $\pm$ 9.3	-	0.58
EtCO₂ (mmHg)	27.7 $\pm$ 3.6	31.3 $\pm$ 6	30.4 $\pm$ 5.5	-	0.07
Vd (mL)	175 $\pm$ 110	127 $\pm$ 88	154 $\pm$ 126	-	0.58
Vd/Vt (%)	25 $\pm$ 9	25 $\pm$ 11	29 $\pm$ 18	-	0.97
Measurements only in patients not on O₂ supplementation					
Patients not on O₂ supplementation #	9 (27)	3 (21)	0 (0)	0 (0)	0.04
TcPO₂ (mmHg)	76 $\pm$ 11	74 $\pm$ 8	82 $\pm$ 12	85 $\pm$ 12	0.049
PaO₂ (mmHg)	78 $\pm$ 11	77 $\pm$ 14	79 $\pm$ 10	-	0.84
PaO₂ - TcPO₂ (mmHg)	1.0 $\pm$ 11.3	3.4 $\pm$ 8.4	-3.7 $\pm$ 8.4	-	0.27
TcPCO₂ (mmHg)	30 $\pm$ 5	37 $\pm$ 7	33 $\pm$ 10	39 $\pm$ 3	<0.001
PaCO₂ (mmHg)	32 $\pm$ 4	42 $\pm$ 4	39 $\pm$ 5	-	<0.001
PaCO₂ - TcPCO₂ (mmHg)	3.0 $\pm$ 3.1	3.6 $\pm$ 3.7	5.1 $\pm$ 9.3	-	0.92
EtCO₂ (mmHg)	28 $\pm$ 4	31 $\pm$ 6	30 $\pm$ 6	-	0.08

Abbreviations: CO₂: carbon dioxide, EtCO₂: end-tidal carbon dioxide, FIO₂: fraction of inspired oxygen, O₂: oxygen, PaCO₂: partial pressure of CO₂ in arterial blood, PaO₂: partial pressure of O₂ in arterial blood, TcPCO₂: transcutaneous carbon dioxide, TcPO₂: transcutaneous oxygen, Vd: physiological dead space, Vt: tidal volume.

Table 3

Correlation table in patients with pulmonary arterial hypertension.

	TcPO ₂ /FiO ₂		TcPO ₂ *	
	R	p	R	p
Cardiac output #	0.37	0.04		
Cardiac index #	0.36	0.049		
TPG	−0.36	0.05	−0.42	0.04
PVR	−0.39	0.03		
SVI	0.46	0.01		
CAMPHOR (activities)	−0.73	0.001	−0.76	0.006
CAMPHOR (QOL)	−0.54	0.03	−0.60	0.049
DLCO (% of predicted)	0.58	0.005		

Only significant associations are shown.

* Only in patients not on O₂ supplementation.

measured by thermodilution.

Abbreviations: CI: cardiac index, DLCO: diffusing capacity of carbon monoxide, PAP: pulmonary artery pressure, PVR: pulmonary vascular resistance, QOL: quality of life, R: Pearson correlation coefficient, SVI: stroke volume index and TPG: transpulmonary gradient.