

Estimates of mean alveolar gas in patients with chronic airways obstruction

A. Giannella-Neto*, P. Paoletti, E. Fornai, C. Giuntini

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ABSTRACT: Alveolar to arterial differences (AaD) may be computed from representative alveolar gas pressures (P_A). These are particularly difficult to obtain in patients with chronic airways obstruction (CAO) and severe inhomogeneity of the ventilation/perfusion (\dot{V}_A/\dot{Q}) ratio. In 25 such patients, using a computerized mass spectrometer, representative values of alveolar gas were obtained: 1. as end-tidal concentrations (ET); 2. using the alveolar air equation with P_{ACO_2} derived from Bohr's equation (BE); 3. putting $P_{ACO_2}=P_{ACO_2}$ into the alveolar air equation to compute ideal O_2 alveolar pressure (ID); 4. applying Rahn's definition of "mean" alveolar gas (RD), i.e. taking within each j th breath, the alveolar pressures corresponding to the moment when the instantaneous gas exchange ratio $R(t)$, equals the overall exchange ratio for that breath R . During quiet breathing, the point where $R(t)$, equals R , occurred at 71% of tidal volume (V_T). Alveolar pressures by BE and RD resulted in similar values (115.5 ± 6.9 and 115.5 ± 6.6 mmHg for O_2 and 30.3 ± 5.7 and 30.8 ± 5.7 mmHg for CO_2 , respectively), but they were significantly different from those by ET and ID (106.2 ± 9.5 and 95.6 ± 13.5 mmHg for O_2 and 36.3 ± 7.7 and 48.2 ± 11.2 mmHg for CO_2 , respectively). These findings may be explained considering that $P_A(BE)$ and $P_A(RD)$ represent both high and low \dot{V}_A/\dot{Q} units, whereas $P_A(ET)$ and $P_A(ID)$ represent mainly low \dot{V}_A/\dot{Q} units. AaD_{CO_2} by RD and BE appeared proportional to the severity of CAO as estimated from V_T . Automated techniques make it possible to substitute end-tidal determinations with more accurate estimates either by measuring anatomical dead-space and using Bohr's equation or by applying Rahn's definition.

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In patients with chronic airways obstruction (CAO), alveolar gas concentration may be greatly uneven due to ventilation to volume, perfusion to volume, and ventilation to perfusion inequalities [1, 2, 3]. Stratified diffusive ventilation may add to this unevenness [1, 4, 5]. During tidal breathing, sampling of alveolar gas is dependent on the size of V_T [6, 7, 8], anatomical dead space [9,10], and asynchronous emptying of air spaces [11]. All these conditions influence to various degrees the methods used for obtaining alveolar gas concentrations.

End-tidal measurements of expiratory gases, though widely used, may hardly be considered representative of the mean alveolar gas. On the other hand, indirect determinations of alveolar gas by Bohr's and ideal alveolar air equations depend on assumptions concerning the dead space. However, since the measurement of the respiratory exchange ratio is independent of the presence in the

expired air of contributions from the dead space, it is possible, as shown by RAHN [12] for normal subjects, to derive from the O_2 - CO_2 diagram the mean alveolar gas as the gas mixture where the "instantaneous" respiratory exchange ratio within a cycle equals the respiratory exchange ratio of that cycle. Obviously, if this occurs when the anatomical dead space is not completely emptied, the values of O_2 and CO_2 derived from the diagram will overestimate and underestimate, respectively, alveolar concentrations. Therefore, our purpose was to investigate whether, in patients with CAO, this method could be applied and yield results comparable with those of the methods mentioned above. Such comparison, attempted by LUFT and co-workers in patients with various pulmonary diseases [13] and by GIANNELLA-NETO and co-workers [14] in patients with pulmonary embolism, yielded substantially similar results for the different

methods. However, both these studies, unlike ours, reported on patients with limited degrees of alveolar gas inequalities. Finally, in the present study of patients mostly with advanced CAO, it seemed of interest to evaluate the results obtained with the different methods by relating them to the severity of the respiratory impairment.

Patients and Methods

Twenty-five patients (23 males and 2 females) with CAO were studied. The patients were characterized on the basis of clinical history, lung function tests by spirometry and body plethysmography, arterial blood gas data, and chest X-ray findings. A clinical history of chronic cough and phlegm, moderate over distension of the lungs, hypoxaemia with CO_2 retention, enlarged heart shadow and prominent broncho-vascular markings were taken as distinctive features of CAO type B [15]. A history of dyspnoea, marked over-distension of the lungs, hypoxaemia without CO_2 retention, small heart shadow and attenuated peripheral vascular markings were considered suggestive for CAO type A [15]. Accordingly, fourteen patients were considered to have mixed features of chronic bronchitis and emphysema, whereas four had the features of chronic bronchitis alone and three of emphysema only. Two patients were considered to have asthmatic bronchitis on the basis of their clinical history and they did not show increase of static lung volumes at the study. One patient had bronchiectasis as assessed at bronchography and one bullous emphysema. Values of lung function tests, reported in table 1, indicate on the average a marked degree of airways obstruction in this series of patients ($\text{FEV}_{1,}$ forced expired volume in first second=34% of predicted). Predicted values were obtained from ULMER for thoracic gas volume (TGV) [16], from MORRIS and co-workers for forced vital capacity (FVC) and FEV_1 [17], and from GOLDMAN and BECKLAKE for vital capacity (VC), functional residual capacity (FRC), and total lung capacity (TLC) [18]. As to the level of hypoxaemia and hypercapnia, it was, on average, the same as in patients being selected for long-term oxygen treatment [19]. The patients were in stable clinical conditions at the time of the study and were not receiving oxygen therapy.

The scheme of the experimental set-up for the measurement of gas exchange is shown in figure 1. Patients in sitting position, with a nose-clip, breathed through a mouthpiece via a Hans-Rudolph valve (34 ml dead space) connected to a pneumotachograph (Fleisch no. 3) for expiratory flow and volume measurements. Respiratory gas and water vapour were analysed by a respiratory mass spectrometer (RMS) (Varian M3). The expired gas was collected in a Douglas bag for analysis. After a few minutes of adaptation and when steady state conditions were reached (see below), computer signals acquisition started for a time interval of 5 min. During one minute a sample of arterial blood was collected by local puncture from the radial artery. Blood gas analysis was performed immediately by the standard electrode method (Instrumentation Laboratory 1302). Constancy of end-

tidal gas concentrations and of expiratory volume on the polygraph recorder was used to assess the presence of steady state conditions. Moreover, the steady state was evaluated later on by comparison between mean respiratory exchange ratio during the arterial blood sample interval and mean respiratory exchange ratio during the whole acquisition interval.

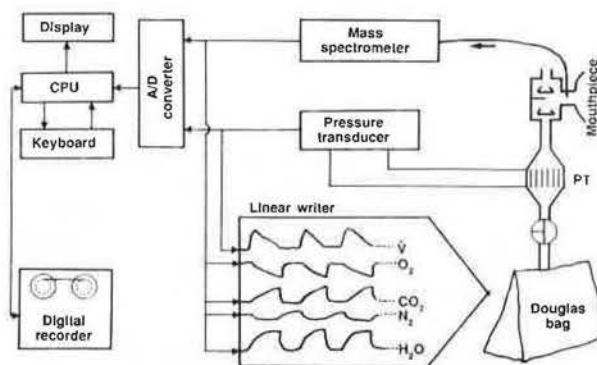


Fig. 1. — Scheme of the experimental set-up to obtain breath-by-breath alveolar gas pressures. CPU: computer processing unit; A/D: analogue to digital; PT: pneumotachograph. N_2 deflections are negative because of the H_2O vapour influence.

Acquisition and processing programmes already reported [20] are as follows. Signals from RMS and flowmeter were fed into a computer (Hewlett-Packard 1000) with 100 Hz sampling rate and stored on magnetic tape with digital recorder (Hewlett-Packard 7970 B) for off-line processing.

Flow and volume were calibrated using a standard syringe (1 litre volume) according to the European Community for Coal and Steel recommendations* and RMS was calibrated by using a known water vapour saturated mixture of gases (O_2 , CO_2 , and N_2).

The processing programme aligned flowmeter and RMS signals on a time basis by computing the time delay between the take off of the expiratory flow signal and that of the water vapour signal.

For each j th breath the following computations were made:

- expiratory tidal volume (VT_j);
- anatomical dead space (VD_{anat}) on expired CO_2 using the Fowler's technique as modified by GUY and co-workers [21];
- inspiratory fractions and pressures ($\text{F}_{i,j}$, $\text{P}_{i,j}$) of gases to check the calibration of RMS;
- end-tidal fractions and pressures of gases ($\text{F}_{\text{ET},j}$, $\text{P}_{\text{ET},j}$);
- expiratory fractions and pressures of gases derived from the numerical integration of concentration time tidal expiratory flow ($\text{F}_{\text{E},j}$, $\text{P}_{\text{E},j}$);
- respiratory exchange ratio (R_j) using fractions computed at point e;

* Standardized Lung Function testing. Ed. Ph.H. Quanjer. *Bull. Europ. Physiopath. Resp.*, 1983, 19 suppl 5, 11-21.

Table 1. - Physical characteristics, arterial blood gases, and lung function parameters in 25 patients with chronic airways obstruction

	Units	Mean	Standard deviation	Range	% of predicted
Age	yrs	62	(9)	45-80	-
Height	cm	166	(6)	149-178	-
Weight	kg	68	(10)	52-95	-
PAO ₂	mmHg	50.7	(8.9)	30-60	-
PACO ₂	mmHg	48.2	(11.2)	29-72	-
V _T	l	0.45	(0.13)	0.23-0.61	-
V _{D_{anat}}	ml	120	(35)	58-178	-
V _{D_{phy}} /V _T	%	52	(8)	37-63	-
VC	l	2.84	(0.82)	1.62-4.51	85
FVC	l	2.48	(0.84)	1.39-4.38	65
FEV ₁	l	0.93	(0.51)	0.41-2.16	34
sGaw	s·cmH ₂ O ⁻¹	0.04	(0.04)	0.17-0.01	-
TGV	l	5.32	(1.68)	2.27-9.30	173
FRC	l	4.70	(1.37)	2.45-7.10	149
TLC	l	6.37	(1.31)	3.46-8.52	118
RV/TLC	%	54	(14)	30-73	144

sGaw: specific airways conductance; RV/TLC: residual volume to total lung capacity ratio; see text for other symbols and references for predicted values.

g. instantaneous respiratory exchange ratio (R(t)).

Using these figures, alveolar O₂ and CO₂ pressures were computed in each jth breath by the following methods:

1. as end-tidal pressures (PAO₂(ET)_j, PACO₂(ET)_j;
2. from Bohr's equation (PAO₂(BE)_j, PACO₂(BE)_j;

$$PACO_2(BE)_j = (V_{Tj} / (V_{Tj} - V_{D_{anatj}})) \cdot PECO_{2j} \quad (1)$$

PAO₂(BE)_j was computed substituting PACO₂(BE)_j from equation 1 into the alveolar air equation:

$$PAO_2(BE)_j = P_{iO_2j} - PACO_2(BE)_j \cdot (F_{iO_2j} + (1 - F_{iO_2j}) / R_j) \quad (2)$$

3. as ideal oxygen pressure (PAO₂(ID)_j;

$$PAO_2(ID)_j = P_{iO_2j} - PACO_2 \cdot (F_{iO_2j} + (1 - F_{iO_2j}) / R_j) \quad (3)$$

with PACO₂ the arterial blood carbon dioxide pressure;

4. according to RAHN's definition of mean alveolar gas [12], (PAO₂(RD)_j, PACO₂(RD)_j;

PAO₂(RD)_j and PACO₂(RD)_j were taken, within each breath, when the computer algorithm found the equality between R(t)_j and R_j [20].

This approach allowed the experimental verification of the theoretical analysis (presented in Appendix) which predicts, at variance with the results of LUFT and co-workers [13], that under steady state conditions, it is always possible to find in any tidal breath the equality between R(t)_j and R_j.

Alveolar gas pressures obtained by the various methods were averaged over the N breaths either of the whole

acquisition time (Nw) or of the arterial blood sampling interval (Ns):

$$PA = (1/N) \sum_{j=1}^N PA_j \quad (4)$$

where PA_j is the alveolar pressure (of O₂, CO₂, and N₂) according to one of the methods mentioned above. Mean expiratory pressures during Ns or Nw were computed as follows:

$$PE = \frac{\left(\sum_{j=1}^N PE_j \cdot V_{Tj} \right)}{\sum_{j=1}^N V_{Tj}} \quad (5)$$

using V_{Tj} and PE_j values calculated at points a, and e, respectively. Expiratory pressures computed in equation 5 were used to calculate the respiratory exchange ratio during the corresponding N breaths (Ns or Nw, respectively).

The programme also computed the following parameters: physiologic dead space to tidal volume ratio (V_{D_{phy}}/V_T) according to the Enghoff modification of Bohr's equation [13], alveolar ventilation (V_A), and minute ventilation (V_E). Computer determinations of O₂, CO₂, and N₂ expiratory fractions and of respiratory exchange ratio during Nw breaths were compared, as already described [20], with measurements of mixed expired gas through Scholander's technique [22].

Alveolar pressure values and gas exchange parameters, reported in the results section, were derived from the Ns breaths corresponding to the arterial blood sampling interval.

Results obtained with the various methods were compared using analysis of variance and Duncan's test [23]. Analysis of correlation was performed using Pearson's linear correlation.

Results

Respiratory exchange ratios during arterial blood sampling, and over the entire acquisition period, were virtually identical, being 0.858 ± 0.09 , and 0.859 ± 0.09 , respectively.

Mean values, and standard deviations for alveolar pressures and alveolar to arterial differences obtained with the various methods are reported in table 2.

neous respiratory exchange ratio of a representative expirogram, obtained during the arterial sampling period, was plotted for each patient against expired volume and expiration time, respectively, in fig. 2. For each patient the representative expirogram is that with respiratory exchange ratio (R_t) equal to mean respiratory exchange ratio during the arterial sampling period. Instantaneous respiratory exchange ratios are represented from bottom to top according to the decreasing value of the respective expiratory tidal volume and independently from their absolute value to lessen visual confusion of curves. The arrowheads indicate the point of equality between $R(t)$ and R_t . It appears that a gas sample with the same respiratory exchange ratio as that of the overall expired gas for one cycle is expired, for a representative breath, within

Table 2. — Comparison by Duncan's test of alveolar gas pressures and alveolar-arterial differences obtained by four methods in 25 patients with CAO

Method	P_{AO_2}		Comparison	p	Method	P_{ACO_2}		Comparison	p
	Mean	SD				Mean	SD		
	mmHg	mmHg				mmHg	mmHg		
BE	115.5	6.9	BE vs RD	ns	BE	30.3	5.7	BE vs RD	ns
RD	115.5	6.6	RD vs ET, ID	0.01	RD	30.8	5.7	RD vs ET	0.05
ET	106.2	9.5	ET vs BE, ID	0.01	ET	36.3	7.7	ET vs BE	0.05
ID	95.6	13.5	ID vs BE	0.01	ID	48.2	11.2	ID vs BE, RD, ET	0.01

Method	AaDo ₂		Comparison	p	Method	aADco ₂		Comparison	p
	Mean	SD				Mean	SD		
	mmHg	mmHg				mmHg	mmHg		
BE	64.8	9.5	BE vs RD	ns	BE	18.0	7.4	BE vs RD	ns
RD	64.8	10.1	RD vs ET, ID	0.01	RD	17.5	7.6	RD vs ET	0.01
ET	55.4	10.9	ET vs BE, ID	0.01	ET	12.0	5.4	ET vs BE	0.01
ID	44.9	11.5	ID vs BE	0.01	ID	"0"	—		

CAO: chronic airways obstruction; BE: Bohr's equation; RD: Rahn's definition; ET: end-tidal; ID: ideal alveolar air equation; SD: standard deviation; p: level of statistical significance; P_{AO_2} and P_{ACO_2} : alveolar oxygen and carbon dioxide gas pressure respectively; Aa: alveolar arterial difference; ns: not significant.

Analysis of variance for P_{ACO_2} and AaDco₂ showed that the methods were significantly different. P_{ACO_2} (RD) and P_{ACO_2} (BE) were not significantly different by Duncan's analysis, but they were both different from P_{ACO_2} (ET). P_{ACO_2} (ID) was different from all the other values. Similar results were obtained when aADco₂ values were considered.

The four methods for measuring P_{AO_2} and AaDo₂ gave significantly different results by analysis of variance. Duncan's analysis showed that P_{AO_2} (RD) and P_{AO_2} (BE) were not significantly different, while they were significantly different from P_{AO_2} (ET) and P_{AO_2} (ID); this latter value was also different from P_{AO_2} (ET). The same results were obtained when AaDo₂ values were considered.

In order to verify the applicability of the measurement of alveolar gas pressures by Rahn's definition during quiet tidal breathing in patients with CAO, the instanta-

the tidal volume during quiet steady state breathing in our patients. In fact, $R(t)$ equals R_t when about 2/3 of the tidal volume are exhaled. On average, this corresponds to an expired volume, expressed as a percentage of the tidal volume, of $71 \pm 9\%$. In practice, it is quite possible that a particular non "representative" spontaneous breath will exhibit $R(t) = R_t$ beyond the mean tidal volume point. In figure 2, the elevated values of the exchange ratio at the beginning of expiration should reflect the very high but non-infinite value of series dead space \dot{V}_A/\dot{Q} ratio [24].

Instantaneous expired fractions of O₂ and CO₂ from the same tidal volume of figure 2 were plotted against time in figure 3 for each patient. The arrowheads locate on each expirogram the point where $R(t) = R_t$. This occurs beyond the knee of the curves where the bulk of the dead space may be considered washed out. Only in 3

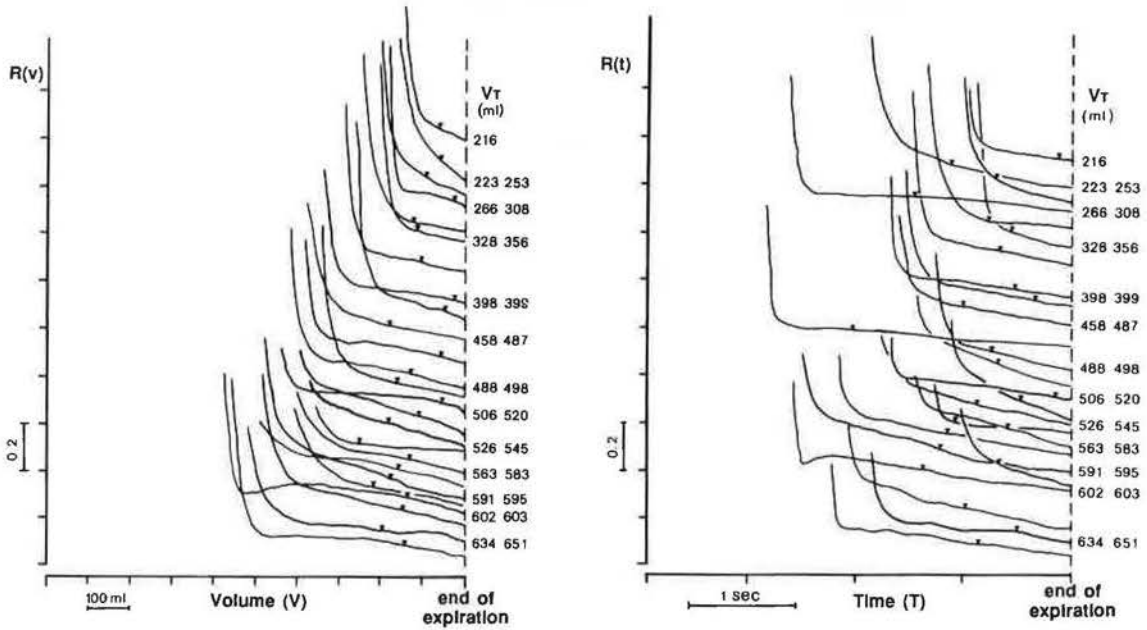


Fig. 2 - Instantaneous respiratory exchange ratios versus volume and time ($R(v)$ and $R(t)$, respectively) for the representative j th expirogram, i.e., that with the respiratory exchange ratio (R_c) equal to mean respiratory exchange ratio during the arterial blood sampling period. Respiratory exchange ratios are ranked from bottom to top according to decreasing tidal volumes and, for graphical clarity, independently from their absolute value. Values of $R(v)$ and $R(t)$ increase from bottom to top by the amount shown on the ordinate. Arrowheads indicate when instantaneous respiratory exchange ratio ($R(t)$, equals R_c). On the left panel, arrowheads correspond on average, to 71% of the expiratory tidal volume. Decreasing values of instantaneous respiratory exchange ratio reflect emptying of lung units with progressively lower \dot{V}_A/\dot{Q} ratios.

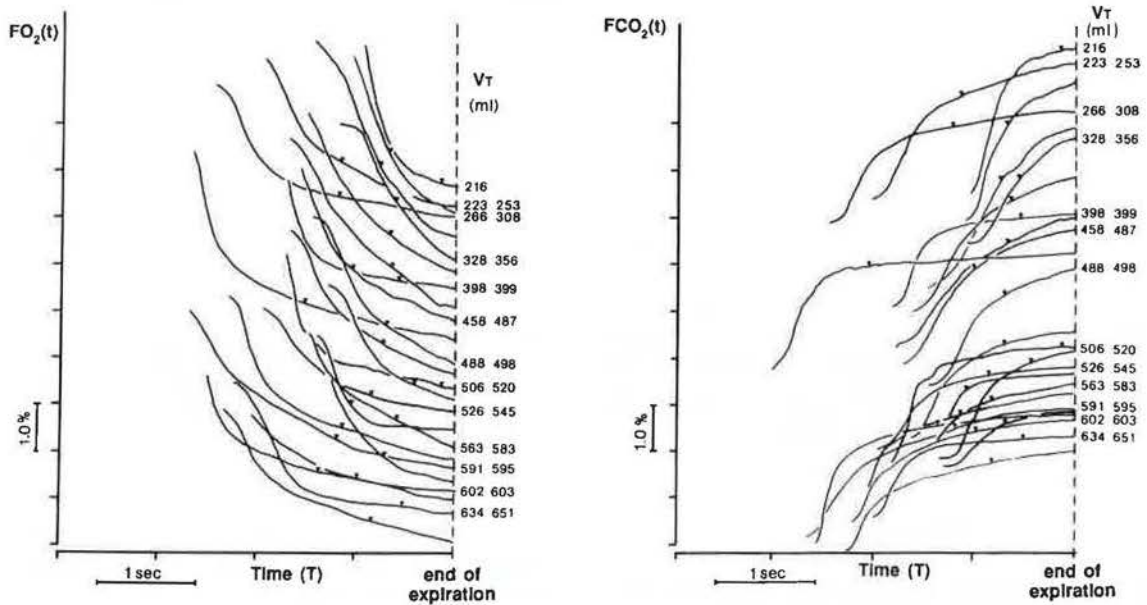


Fig. 3. - O_2 and CO_2 expiratory fractions, as a percentage, on the ordinate for the same respiratory cycles represented in figure 2. Arrowheads and ranking of tracings have the same meaning as in figure 2. For graphical clarity individual expirograms are plotted independently from absolute value of O_2 and CO_2 fractions. For each expirogram, O_2 and CO_2 fractions increase from bottom to top by the amount shown on the ordinate.

curves, with V_T of 253, 308, and 328 ml respectively, the knee is ill defined and it is possible that at the aforementioned point some contribution of gas from the anatomic dead space is still contaminating the expired alveolar gas.

To evaluate the relationships between gas pressures and tidal volume, O_2 and CO_2 alveolar pressures by the various methods, with the exclusion of the ideal air method, were plotted against tidal volume in figure 4.

Significant correlations are always present.

Finally, O_2 and CO_2 alveolar-arterial differences by the same methods were plotted against tidal volume in figure 5. Negative correlations are present for CO_2 alveolar-arterial difference for all the methods; however, only the correlations with RD and BE methods were significant. With regard to the O_2 alveolar-arterial difference, none of the correlations were significant.

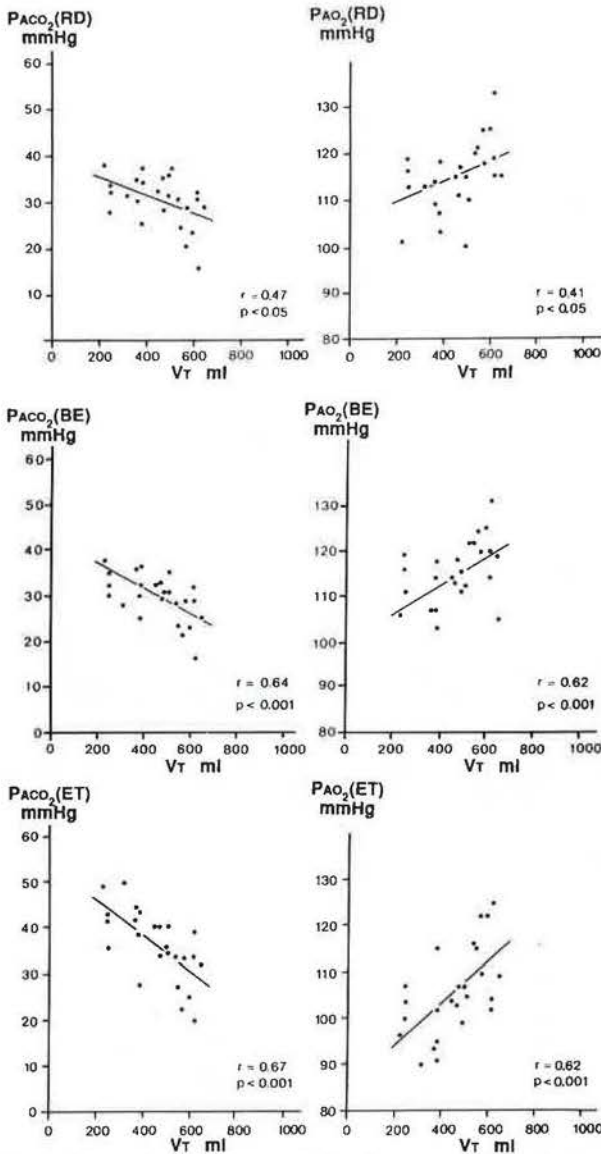


Fig. 4. - Regressions of CO₂ and O₂ alveolar pressures (PA), obtained from Rahn's approach (RD), Bohr's equation (BE), and as end-tidal values (ET), respectively, against expiratory tidal volume in 25 patients with chronic airways obstruction. Correlation coefficient and level of significance are reported in each diagram.

Discussion

Steady-state conditions should be first considered. The effect of arterial blood sampling apparently did not disturb the mode of breathing of our subjects since there was no change in the respiratory exchange ratio between this period and the entire study period. Indeed, neither the average value nor the standard deviation showed any difference between the two periods. Measurement of gas exchange based on the determination of the expiratory V_T alone may leave some uncertainty about the stability of FRC. This has been the subject of considerable controversy in the current literature [25-28]. The conclusions of GIEZENDANNER and co-workers [26] that "mean resting and steady-state exercise gas exchange data cor-

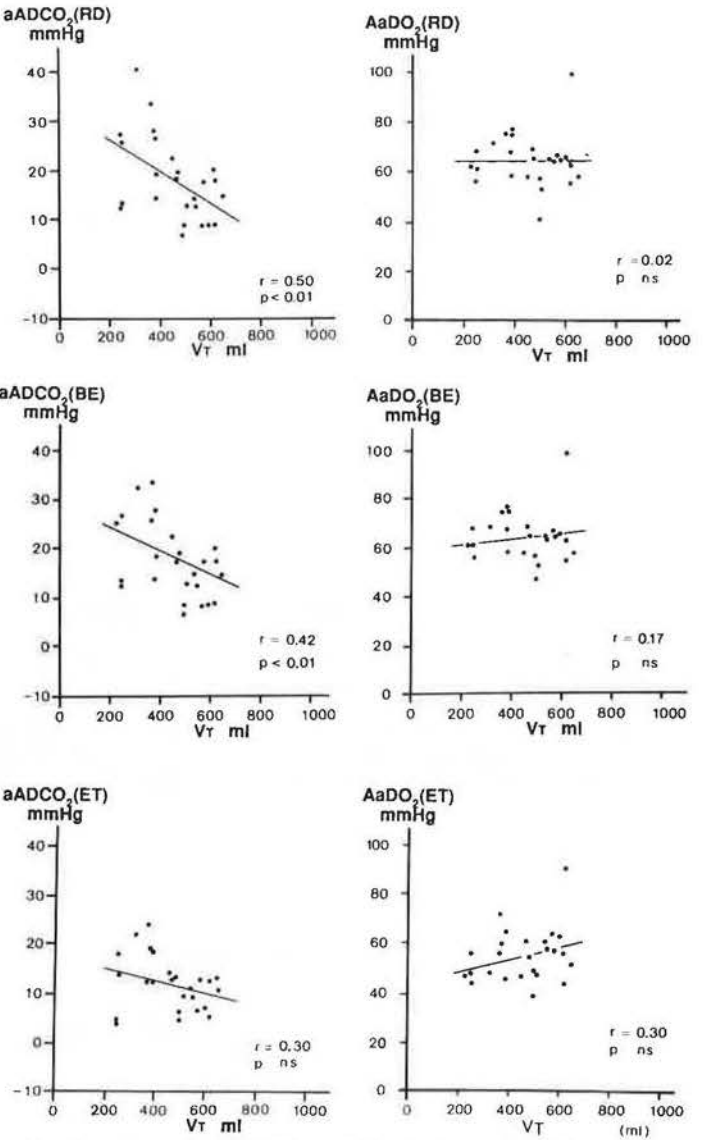


Fig. 5. - Regressions of CO₂ and O₂ alveolar-arterial differences, obtained according to Rahn's approach (RD), Bohr's equation (BE), and end-tidal measurements (ET), respectively, against expiratory tidal volume (V_T). Correlation coefficient and level of significance are reported in each diagram. ns: not significant.

rected for changes of lung gas stores are equal to those obtained by conventional open-circuit measurements" seem to apply to our patients since they are not likely to change the level of FRC and the respiratory gas exchange ratio was remarkably constant throughout our study. On the other hand, as indicated in the Appendix, the instantaneous respiratory gas exchange ratio can be defined only in presence of steady-state N₂ balance.

During steady-state quiet breathing in patients with CAO, the pressures of CO₂ and of O₂ in the end-tidal estimates were higher and lower, respectively, than those derived with Bohr's equation and Rahn's approach. These findings may be ascribed to the particular shape of the concentration time curve of the respiratory gases at the mouth in these patients (fig.3.). The significant

difference between the values is at variance with the data reported by LUFT and co-workers [13]. The data of these authors, however, aside from technical differences, *e.g.* sequential rather than simultaneous application of Rahn's approach, application of the latter on a single extended expiration, and use of predicted rather than measured values for anatomic dead space, pertain to patients with a lower degree of air flow obstruction.

Estimates of alveolar CO_2 and O_2 pressures may be influenced by the size of the tidal volume. Indeed, a significant correlation was observed between CO_2 and O_2 pressures on one side, and V_T on the other (fig. 4). End-tidal pressures and alveolar pressures derived using Bohr's equation (equation 2) showed correlation coefficients higher than those obtained using alveolar pressures derived with Rahn's approach. These results are not surprising since Bohr's derivation is directly dependent on V_T and end-tidal pressures in patients with CAO represent mainly lung units at low \dot{V}_A/\dot{Q} with alveolar pressures depending characteristically, especially in bronchitic type patients, on V_T [8]. With Rahn's approach, V_T does not enter directly into the calculations as in Bohr's derivation. Thus, alveolar pressures estimated according to Rahn's approach reflect also the contribution of high \dot{V}_A/\dot{Q} units, which seem to play an important role in CAO [29–31], and may have a higher degree of variance with respect to V_T than those estimated with the other two methods.

As to the accuracy of the estimates derived with Bohr's equation and Rahn's approach, it should be pointed out that they depend respectively, on the correct prediction or measurement of the anatomic dead space and complete washout of this space at $R(t)=R_i$. As to the Bohr's equation, the prediction of the anatomic dead space may be critical especially at low V_T . Indeed, the use of the anatomic dead space, predicted according to HART and co-workers [32], to obtain PACO_2 (BE) yielded exceedingly low and even negative values of $a\text{ADCO}_2$ (BE) at very low V_T . These paradoxical results suggest that this predicted value of $V_{D_{\text{anat}}}$ may be too high and not applicable in our patients. As a matter of fact, our measured values of $V_{D_{\text{anat}}}$ resulted lower than those predicted according to HART and co-workers [32] (fig. 6). This is in agreement with the observations of BARNIKOL and co-workers [33] who found a reduction of the anatomic dead space in patients with CAO. Finally, the Fowler's technique as modified by GUY and co-workers [21] resulted in little sensitivity to possible errors in interpolating the final portion of the alveolar plateau of the expirograms of our patients. Interpolation at 60 or 80% of the expired V_T , in the expirograms with the 6 lowest V_T including the 3 with the mentioned ill definition of the knee, decreased or increased $V_{D_{\text{anat}}}$ respectively by less than 5 ml with respect to an average interpolation at 70% of expired V_T . The corresponding change in PACO_2 (BE) was less than 1 mmHg, *i.e.* a negligible quantity. These results suggest that $V_{D_{\text{anat}}}$ and PACO_2 (BE) may be measured with sufficient accuracy in patients with severe CAO.

As to Rahn's approach, since $R(t)=R_i$, when the expired CO_2 and O_2 pressures are following a virtually

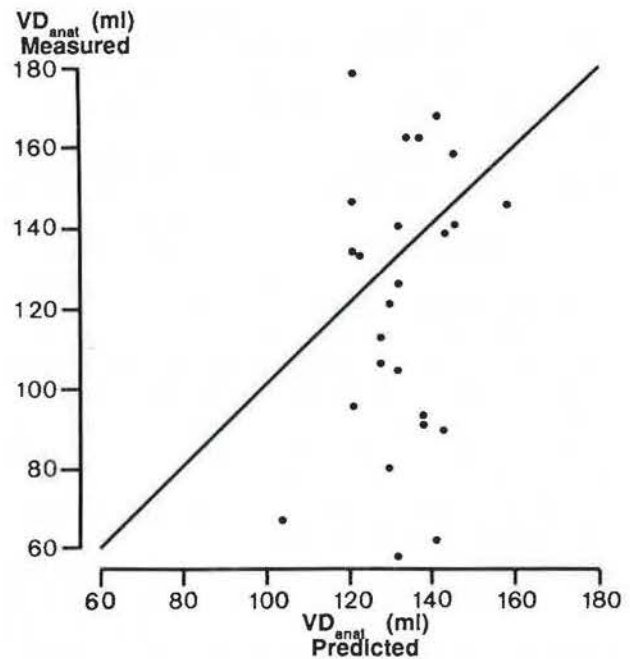


Fig. 6. – Anatomical dead space ($V_{D_{\text{anat}}}$) measured on expired CO_2 using the Fowler's technique, as modified by GUY and co-workers [21], versus $V_{D_{\text{anat}}}$ predicted according to HART and co-workers [32]. The values are widely scattered around the identity line and do not correlate. Measured values (120 ± 34 ml) were, on average, lower than those predicted (133 ± 11 ml) but showed a considerably wider range (58 to 178 and 104 to 158, respectively).

straight line pattern (fig. 3.), only slightly contaminated alveolar gas may be sampled at this time. Indeed, the condition that V_T be equal or higher than 10% of vital capacity, postulated by BARGETON and co-workers [7] in order to have, at $R(t)=R_i$, an expired volume composition not contaminated by dead space, was satisfied in our patients. At any rate, even in the case when the dead space has not been completely washed out [9,10], the curves of figures 2 and 3 indicate that its contribution to the expirate may be very small at $R(t)=R_i$. Since at this point 320 ml, *i.e.* 71% of V_T on average, have been expired, a volume equal to $V_{D_{\text{anat}}}$ (see table 1) has been renewed 2.67 times. Assuming complete mixing between $V_{D_{\text{anat}}}$ and V_T , which is the most unfavourable case for the exhalation of $V_{D_{\text{anat}}}$, the amount of the latter yet to be expired corresponds to about 8 ml. These computations suggest that the contamination of the last 29% of V_T , *i.e.* 130 ml on average, by $V_{D_{\text{anat}}}$ may be at most a few percent.

Similar consideration may apply to the effect due to the duration of the respiratory cycle especially since, unlike LUFT and co-workers [13], we are dealing with spontaneous cycles and not extended expiration breaths. Hence, the effect due to continuing respiratory gas exchange if minimal.

The alveolar-arterial differences calculated from the alveolar pressures obtained by the different methods show some interesting features (fig. 5.). The CO_2 pressure

differences derived by Bohr's equation and Rahn's approach present significant negative correlation with the size of V_T suggesting that, in patients with CAO, the decrease of V_T is not only an index of decreased alveolar ventilation [8] but of wasted ventilation. Even the CO_2 difference computed from the end-tidal values exhibits a trend towards decrease when V_T increases but the correlation is not statistically significant.

The O_2 pressure differences derived with all the methods (including $AaDO_2$ (ID) not shown in fig. 5) were not significantly related to the size of V_T . Therefore, it appears that O_2 difference is independent of V_T in patients with CAO. Implicit in these findings is the different meaning of the CO_2 and O_2 differences in patients with CAO. Both CO_2 and O_2 gradients should then be obtained to characterize these patients and to follow them through the years and the various treatments.

Mean alveolar CO_2 and O_2 pressures derived, in patients with severe CAO, by Bohr's equation and Rahn's approach were virtually identical, even if the methods differ in several respects. On the other hand, the alveolar gas pressures measured by these two methods differed significantly from the end-tidal gas pressures. In physiological terms, such a difference may be explained considering that $PA(BE)$ and $PA(RD)$ reflect the contributions to expiratory flow of units with both high and low \dot{V}_A/Q ratios, whereas $PA(ET)$ reflect mainly the contribution to expiratory flow of units with low \dot{V}_A/Q ratio. From the practical point of view, our results suggest that the widely used end-tidal gas concentrations may be very misleading in patients with CAO. The increased availability of automated techniques [7, 20, 21] should make possible the substitution of end-tidal determinations with the more accurate measurements. Since predictive formulae may overestimate anatomic dead space in patients with CAO, either $V_{D_{anat}}$ is measured or Rahn's approach, which does not require knowledge of its size, is used.

Appendix

It was postulated by LUFF and co-workers [13] on empirical grounds, that the point on the O_2 - CO_2 diagram where $R(t)_j=R_j$, essential in the Rahn-Bargeton method of obtaining mean alveolar gas [6, 12], "does not fall within the tidal volume in many patients and can only be obtained by an extended expiration" [13]. We wished to verify whether this was to be expected on theoretical grounds.

Considering N_2 net balance to be null in each breath or $F_{IN_2} \cdot V_{TI} = F_{EN_2} \cdot \dot{V}_T$, where V_{TI} is the inspired tidal volume (V_T throughout the paper is the expired tidal volume), we can demonstrate that in each j th breath there is, at least, one point where $R(t)_j = R_j$.

$$\text{Let} \quad a(t) = F_{ECO_2}(t) - (F_{ICO_2}/F_{IN_2}) \cdot F_{EN_2}(t) \quad A1$$

$$\text{and} \quad b(t) = (F_{IO_2}/F_{IN_2}) \cdot F_{EN_2}(t) - F_{EO_2}(t) \quad A2$$

and $f(t)$ = instantaneous expired flow.

Assuming $t=0$ as the instant for start of expiration, $t=T$ as the end-tidal instant, and the instantaneous expired flow arbitrarily positive, it follows that:

$$\left. \begin{array}{l} a(t) \geq 0 \text{ for } 0 < t < T \\ b(t) \geq 0 \text{ for } 0 < t < T \\ f(t) \geq 0 \text{ for } 0 < t < T \end{array} \right\} \quad A3$$

Instantaneous respiratory exchange ratio $R(t)$ for the j th breath is the ratio:

$$R(t)_j = a(t)/b(t) \quad A4$$

and mean respiratory exchange ratio for the same breath is

$$R_j = \int_0^T a(t) \cdot f(t) \cdot dt / \int_0^T b(t) \cdot f(t) \cdot dt \quad A5$$

where the numerator equals carbon dioxide output (\dot{V}_{CO_2j}) and the denominator equals oxygen uptake (\dot{V}_{O_2j})

$$\text{From A4} \quad a(t) = R(t)_j \cdot b(t) \quad A6$$

and substituting A6 in A5 produces

$$R_j = \int_0^T R(t)_j \cdot b(t) \cdot f(t) \cdot dt / \int_0^T b(t) \cdot f(t) \cdot dt$$

$$\text{or} \quad \int_0^T R_j \cdot b(t) \cdot f(t) \cdot dt = \int_0^T R(t)_j \cdot b(t) \cdot f(t) \cdot dt$$

$$\text{or} \quad \int_0^T [R_j - R(t)_j] \cdot b(t) \cdot f(t) \cdot dt = 0 \quad A7$$

Considering the inequalities A3 and as the functions $a(t)$, $b(t)$, and $f(t)$ are not trivial and continuous, with first derivatives finite in the interval $0 < t < T$, it follows that the term $[R_j - R(t)_j]$ has to change sign in the considered time interval to satisfy the condition of nullity for the definite integral.

Obviously, there will exist a time instant (t_{RD}) where $R(t_{RD})_j = R_j$. This t_{RD} that satisfies Rahn's definition is always present if the analysis is performed on a breath by breath basis in quiet breathing steady-state conditions.

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- Estimation des gaz alvéolaires moyens chez des patients atteints d'obstruction chronique des voies aériennes.* A. Giannella-Neto, P. Paoletti, E. Fornai, C. Giuntini.
 RÉSUMÉ: Les différences alvéolo-artérielles (AaD) peuvent être calculées à partir des pressions représentatives des gaz alvéolaires (P_A). Celles-ci sont particulièrement difficiles à obtenir chez les patients atteints d'obstruction chronique des voies aériennes (CAO) et d'inhomogénéité sévère de leur rapport ventilation/perfusion (\dot{V}_A/\dot{Q}). Chez 25 patients de ce type, nous avons obtenu des valeurs représentatives des gaz alvéolaires par l'utilisation d'un spectromètre de masse informatisé: 1. sous forme de concentrations à la fin du volume courant (ET); 2. en utilisant l'équation de l'air alvéolaire avec la P_{ACO_2} obtenue à partir de l'équation de Bohr (BE); 3. en plaçant dans l'équation de l'air alvéolaire $P_{ACO_2} = P_{ACO_2}$ pour calculer la pression alvéolaire idéale en O_2 (ID); 4. en appliquant la définition de Rahn concernant le gaz alvéolaire "moyen" (RD), c'est-à-dire en prenant, à l'intérieur de chaque respiration jth, les pressions alvéolaires correspondant au moment où le rapport des échanges gazeux instantanés $R(t)$, égale le rapport des échanges globaux pour cette respiration R_j . Au cours de la respiration calme, le point où $R(t)_j$ égale R_j est apparu à 71% du volume courant (V_T). Les pressions alvéolaires par BE et RD ont donné des résultats similaires (115.5 ± 6.9 et 115.5 ± 6.6 mmHg pour O_2 et 30.3 ± 5.7 et 30.8 ± 5.7 mmHg pour CO_2 , respectivement), mais elles étaient significativement différentes de celles obtenues par ET et ID (106.2 ± 9.5 et 95.6 ± 13.5 mmHg pour O_2 et 36.3 ± 7.7 et 48.2 ± 11.2 mmHg pour CO_2 , respectivement). Ces observations peuvent s'expliquer en considérant que P_A (BE) et P_A (RD) représentent à la fois des unités avec des rapports \dot{V}_A/\dot{Q} élevés et bas, alors que P_A (ET) et P_A (ID) représentent principalement des unités avec rapport \dot{V}_A/\dot{Q} bas. Les aADCO₂

obtenues par RD et BE apparaissent proportionnelles à la gravité de l'obstruction chronique des voies aériennes, estimée à partir du volume courant V_T . Des techniques automatisées permettent de substituer aux déterminations à la fin du volume

courant, des estimations plus précises, soit par une mesure de l'espace mort anatomique et l'utilisation de l'équation de Bohr, soit par l'emploi de la définition de Rahn.
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