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A new method for noninvasive bedside determination of pulmonary blood flow

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Abstract—*A method is presented for determining the pulmonary blood flow from measurements of the time-averaged end-tidal pCO_2 and the CO_2 output.*

The novel technique is based on a formula that is derived from Fick's principle in such a way that it allows a direct calculation of the lung perfusion from simultaneously measured changes in end-tidal pCO_2 and CO_2 output.

These changes are induced by altering the ventilation pattern of the patient for short (30 s) periods of time. Different ways of doing this are discussed and it is shown that a bidirectional change in ventilation, involving hyper- and hypoventilation patterns, most adequately corresponds to the formula derived.

The method has been validated by comparison with cardiac output data obtained by thermodilution. Forty-two measurements were performed during mechanical ventilation on five dogs and six patients with essentially healthy lungs. Lung perfusion was in the range 0·4–6·5 l/min. We found that $Q_{CO_2} = 0{\cdot}97\ Q_{thermo}$ with a s.d. = 18%. The reproducibility of individual measurements was better than 0·3 l/min.

Keywords—*Carbon dioxide, CO_2 output, End tidal pCO_2, Hyperventilation, Hypoventilation, Pulmonary blood flow*

1 Introduction

FICK's principle applied to the O_2 uptake in the lung provides a standard method for measuring the systemic cardiac output. While this technique gives reliable results, it has to be performed with direct measurement of the mixed venous O_2 content and thus requires cardiac catheterisation. To avoid this drawback, noninvasive techniques have been described, applying Fick's principle instead to the CO_2 elimination in the lung. Two approaches for estimating the mixed venous CO_2 content are in current use. Either a rebreathing procedure is employed or the estimation relies on an analysis of a single-breath, CO_2 partial pressure recording (CAMPBELL, HOWELL, 1962; COLLIER, 1956; DEFARES, 1958; HLASTALA *et al.*, 1972; KIM *et al.*, 1966; FARHI *et al.*, 1976).

Common to many of these CO_2 methods is the fact that the arterial and the mixed venous CO_2 content are established by separate procedures. Therefore, systematic errors in each procedure cumulate when calculating the arteriovenous difference $C(a-\bar{v})_{CO_2}$. This is unfortunate since $C(a-\bar{v})_{CO_2}$ is usually small and thus the error in the cardiac output becomes large. As an example, for a difference between mixed venous

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and arterial pCO_2 of about 0·8 kPa (6 mm Hg), an error of only ~0·13 kPa (1 mm Hg) in the individual blood gas estimates may result in 25% error in the cardiac output value.

Another problem associated with previous methods is that they involve rather intricate experimental setups and require time-consuming evaluation of the measured data. Furthermore, the equipment has sometimes to be adjusted to the patient for optimal performance and patient cooperation is frequently assumed. All this makes it difficult, if not impossible, to use present noninvasive techniques for patients on mechanical ventilators.

The aim of this work is to provide a method for determining lung perfusion that is truly simple to carry out and yields the result immediately from a simple calculation or a nomograph. The ambition is to provide a means for online routine measurements especially on mechanically-ventilated patients who do not necessarily have healthy lungs.

2 Theory

2.1 *Background*

KNOWLES *et al.* (1960) have presented a potentially accurate way of obtaining the arteriovenous difference in pCO_2. They measured the change in alveolar pCO_2, P_{ACO_2} for different breath-holding times. These experiments, yielding $\frac{d}{dt}(P_{ACO_2})$, were repeated with different CO_2 concentrations in the inspired gas, thereby changing the P_{ACO_2} working point. The plot $\frac{d}{dt}(P_{ACO_2})$ vs P_{ACO_2} turned out to be a straight line, in accordance with the results of DUBOIS and coworkers (1952). This line has the equation

$$\frac{dP_A}{dt} = \text{constant} \times \frac{\dot{Q}}{V_A} \times (P_{\bar{v}} - P_A), \quad . \quad . \quad . \quad (1)$$

where $P_{\bar{v}}$ is the mean oxygenated mixed venous CO_2 tension, $\dot{Q}$ is the cardiac output and V_A is the equivalent alveolar lung volume. In eqn. 1 and in the following, the subscript 'CO_2' is omitted and all quantities are assumed to refer to carbon dioxide.

As seen from eqn. 1 $P_{\bar{v}}$ can be obtained from the intercept of the straight line with the P_A-axis, where $dP_A/dt = 0$. Although the value of the constant in eqn. 1 can also be calculated, the equivalent volume is an unknown quantity and therefore the lung perfusion cannot be obtained in this way. The present method is an extension of the ideas on which the work of KNOWLES *et al.* is based (GEDEON, 1977; GEDEON, 1979). The problem with the unknown equivalent lung volume encountered by KNOWLES *et al.* is circumvented by measuring the CO_2 output (that is $\frac{d}{dt}(V_A \times P_A)$) instead of the rate of change in P_A with time (that is $\frac{d}{dt}P_A$). Furthermore, to adapt the method to easy clinical use, the P_A working point is altered by a properly performed change in the ventilation pattern instead of adding CO_2 to the inspired gas.

2.2 *Derivation of a formula for the pulmonary blood flow* $\dot{Q}$

Consider Fick's equation for the CO_2 balance in the lung

$$\dot{V} = \dot{Q} \times (C_{\bar{v}} - C_a), \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

where $C_{\bar{v}}$ and C_a stand for the mixed venous and the arterial CO_2 content, and $\dot{V}$ is the CO_2 output. Eqn. 2 can be rewritten by making use of the CO_2 dissociation curve, that is, the content C vs the partial pressure P relation

$$C = C(P). \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

Eqn. 2 becomes

$$\dot{V} = \dot{Q} \times S \times (P_{\bar{v}} - P_a) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

where S is the slope of the dissociation curve evaluated in between the arterial and the mixed venous CO_2 tensions

$$S = \left(\frac{dC}{dP}\right) \quad \text{at} \quad P = \frac{P_{\bar{v}} + P_a}{2}. \quad . \quad . \quad . \quad . \quad . \quad (5)$$

$P_{\bar{v}}$ and P_a are the mean oxygenated mixed venous and the arterial CO_2 tensions, respectively (KNOWLES *et al.*, 1960).

Using the mathematical expression given by eqn. 14 in Appendix 1 for the dissociation curve, we may calculate directly the difference in CO_2 content for the partial pressures $P_{\bar{v}} = 6{\cdot}133$ kPA (46 mm Hg) and $P_a = 5{\cdot}333$ kPa (40 mm Hg). The value obtained is 2·839 vol%. Calculating the same quantity from the partial pressure difference multiplied by the slope factor S (according to eqn. 4) gives 2·840 vol%. Thus eqn. 4 is a very good approximation of eqn. 2.

We now consider a sudden change $dP_a = P_{a1} - P_{a2}$ in the arterial tension. It is here assumed that mixed venous pCO_2 has the same value for the two arterial tensions P_{a1} and P_{a2}.

The immediate change in CO_2 output $d\dot{V}$ is obtained by differentiating eqn. 4

$$d\dot{V} = -\dot{Q} \times S \times dP_a, \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

where S is assumed to be unaffected by the small change in P_a. Since S is a slowly varying function of P, this approximation is accurate for most practical purposes.

The two most important advantages of using eqn. 6 instead of eqn. 4 to calculate $\dot{Q}$ are immediately apparent.

Firstly, $P_{\bar{v}}$ no longer appears explicitly in eqn. 6. It is only in the evaluation of the slope factor S that $P_{\bar{v}}$ must be considered. The impact of this property of eqn. 6 on the accuracy of the calculation of $\dot{Q}$ is considerable. As an example, an uncertainty in the estimated value of $P_{\bar{v}}$ of about 0·53 kPa (4 mm Hg) will give an error of only about 6% in $\dot{Q}$. This error comes from the change in the factor S in eqn. 6 as a result of the error in $P_{\bar{v}}$. The calculation is based on the formulae given in Appendix 1.

Second, only changes and not absolute values of $\dot{V}$ and P_a are to be measured accurately. This puts less stringent requirements on the absolute calibration of the CO_2-concentration recording equipment. More important, it admits an indirect measurement of P_a and thereby allows for a noninvasive procedure. To see this we may write P_a in the form

$$P_a = P_{ET} + E \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

where P_{ET} denotes the end tidal CO_2 partial pressure and E is simply an unknown quantity which in general has positive values. Rewriting eqn. 7 in the form

$$E = (P_a - P_A) + (P_A - P_{ET}) \quad . \quad . \quad . \quad . \quad . \quad . \quad (8)$$

one can interpret E, the difference between end tidal and arterial CO_2 tension, as a sum of the $(a-A)$ difference (first term eqn. 8) due to regions having a $\dot{V}/\dot{Q}$-distribution corresponding to ventilation perfusion ratio $\ll 1$ and the $(A-ET)$ difference (second term in eqn. 8) due to the alveolar dead space with ventilation perfusion ratio $\gg 1$ and the mixing conditions of the alveolar gas.

Assuming that the previously mentioned change in P_a is achieved without affecting E, it follows that

$$dP_a = dP_{ET} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (9)$$

How to ascertain the validity of the assumptions made above will be discussed below.

According to eqn. 9 we can replace dP_a in eqn. 6 by dP_{ET} and we can also eliminate P_a in eqn. 5 by using eqn. 7. This gives us a formula with parameters that can be measured in a noninvasive way.

$$\dot{Q} = -\frac{1}{S} \times \frac{d\dot{V}}{dP_{ET}} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (10)$$

Although the slope of the dissociation curve S is a slowly varying function of the CO_2 parameters, we refrain from assuming that it is a constant. Details of the calculation of a more general form of S will be found in Appendix 1. The final result is

$$\dot{Q} = -\left(\frac{1}{K_0} + \frac{1}{K_1}\left(P_{ET} + E - \dot{V} \times \tfrac{1}{2} \times \frac{dP_{ET}}{d\dot{V}}\right)\right)\frac{d\dot{V}}{dP_{ET}} \quad . \quad . \quad . \quad . \quad (11)$$

where K_0 and K_1 are constants determined by the dissociation curve. In Appendix 1 it is shown that $K_0 = 0{\cdot}332$ and $K_1 = 0{\cdot}228$ may be used for all practical purposes.

For E the value of 0·53 kPa ($\sim$4 mm Hg) is chosen somewhat arbitrarily. However, using this value in eqn. 11, any clinically observed value between 0–1·06 kPa (0–8 mm Hg) will give, as before, less than 6% error in $\dot{Q}$. Thus a broad range of end tidal-arterial pCO_2 differences can be accounted for.

A nomogram-like technique can be developed to eliminate the need to calculate $\dot{Q}$ from eqn. 11. A simple geometrical construction and a special graduated arc are all that is needed to obtain the lung perfusion in this case. The graphical procedure is explained in Appendix 2.

3 Realisation

Turning to the question of how to produce a change in P_a without affecting $P_{\bar{v}}$ and E, it should be remembered that eqn. 11 is derived without any specific assumption about the method chosen. One obvious way is to add CO_2 to the inspired gas. Measurements of P_{ET} and $\dot{V}$ made before the effect of recirculation is observed on $P_{\bar{v}}$ could be used to calculate the pulmonary blood flow. One advantage of this technique would be that large changes in P_a and $\dot{V}$ are easily achieved. On the other hand the measured $\dot{V}$ has to be corrected for the added CO_2, which could be a considerable source of error. Moreover, special equipment would be required to perform these measurements.

In this work we have used another approach that can be readily applied in a clinical setting. The basic idea is to change the length of the pause between inspiration and expiration but to keep the tidal volume, the inspiratory and the expiratory time constant. The example shown in Fig. 1 demonstrates

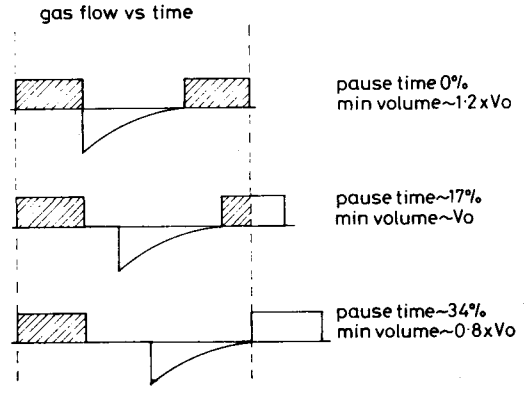

Fig. 1 Illustration of how a variation in the pause time gives changes in the minute volume although the tidal volume, the inspiratory and the expiratory times remain the same. The area under the flow vs time curve corresponds to the volume delivered

that this scheme is equivalent to changing the minute volume and will therefore bring about rapid changes in P_{ET} and $\dot{V}$. The pause time between inspiration and expiration can be regarded as a very short, mandatory breath-holding period. Therefore one may say that the ventilatory change suggested to produce the changes in P_{ET} and $\dot{V}$ amounts to a repeated, well controlled breath-holding procedure of short duration that can be implemented using existing respiratory equipment. Since the expiratory time is kept constant, P_{ET} values are recorded at comparable points on the alveolar plateau even in a case when the CO_2 partial pressure vs time curve does not level off at the end of the expiration. Since the tidal volume is not changed, the peak pressure in the lung remains the same and the mean intrathoracic pressure is also almost unaffected. The change in this parameter may be estimated to be about 7% of the peak pressure value for + 50% change in minute volume. The maintenance of constant pressure conditions is important since, if the pressure in the lung was allowed to alter from one ventilation pattern to another, adverse effects could result, such as a change in the cardiac output or in the equivalent alveolar volume.

A change from a steady-state ventilation pattern to a hyperventilation pattern such as from minute volume V_0 to $1{\cdot}2V_0$, shown in Fig. 1, is in accordance with the rules discussed above. The difference between arterial and end tidal pCO_2 will not be significantly affected and thus our assumption on which eqn. 9 is based is expected to be valid. The most obvious way to perform a lung-perfusion measurement would therefore be to use the two CO_2-parameter values observed for the steady-state ventilation pattern together with the two CO_2 values obtained after a short period of hyperventilation to calculate $\dot{Q}$ from eqn. 11. However, in order not to violate the other of our two assumptions, namely that mixed venous pCO_2 has the same value when recording the CO_2 data of the two ventilation settings, the hyperventilation period must be short enough compared with the system's recirculation time. Recirculation due to hyperventilation tends to lower the $P_{\bar{v}}$ value, which would lead to falsely low values for the calculated lung perfusion.

To minimise the effect of recirculation, a procedure involving a hyperventilation period followed by a hypoventilation period (see pattern with minute volume $0{\cdot}8V_0$ in Fig. 1) appears more attractive. Such a bidirectional deviation from steady state is an advantage in that mixed venous pCO_2 tends to return to the same value at the end of the hypoventilation period as it had at the end of the hyperventilation period. This value may now differ from the initial steady state $P_{\bar{v}}$ and the calculation of $\dot{Q}$ is therefore based on the CO_2 parameters of the hyper- and the hypoventilation settings, while the steady state CO_2 values are not used.

Recirculation will primarily affect the measured change in P_{ET}. Therefore one can say, in general, that for large changes in P_{ET} (that is, for low values for the lung perfusion) our method is more accurate than for small changes in P_{ET} (large perfusion values).

We have measured $\dot{Q}$ both by the steady-state hyperventilation approach and by the hyper-hypoventilation procedure described above. Changes in pause time corresponding to minute volume changes from 20% up to 100% of the basal value have been implemented.

4 Application of the method

All measurements were carried out using a ventilator (Siemens–Elema Servo Ventilator 900 B) and a CO_2 analyser (a slightly modified Siemens–Elema CO_2 Analyzer 930). The ventilator can be set to give predetermined inspiratory and pause-time fractions. Thus different ventilator settings, for instance such as those shown in Fig. 1, could be realised. A small deviation from the constant inspiration time condition had to be accepted in some cases. The electronic ventilator provides instantaneous expiratory flow monitoring at a.t.p.s. conditions and the fast response (response time 6 ms) CO_2 analyser measures the CO_2 partial pressure with no time delay close to the airway opening (at a point between the patient and the Y-piece). Connecting these two pieces of equipment together allows a direct multiplication of the flow curve with the partial pressure curve which, after integration with respect to time, yields the tidal CO_2 output. Thus for each breath one has the tidal output and the end tidal value (which is defined as the maximal partial pressure value during expiration). With a slight modification of the standard CO_2 analyser one can get a display of the time-averaged CO_2 output (expressed in ml/min) and the corresponding time-averaged P_{ET} (in kPa). The averages are taken by analogue electronic circuitry with a 90% response in about 20 s. The averaged values are displayed and updated every breath.

Reference measurements of cardiac output were done, using a thermodilution computer (Instrumentation Laboratories 701), in five dogs (19–34 kg weight) during thiopental anesthesia, and in six patients during neurolept anaesthesia prior to coronary bypass surgery. The thermodilution data were recorded as the mean of three consecutive measurements. In dogs, cardiac output usually decreased slowly with time during the measurements. To obtain a greater range in cardiac output, some dogs were also subjected to stepwise controlled bleeding. The data were taken using the ventilation patterns discussed before.

The length of the hyperventilation was always 30 s, while the hypoventilation period lasted 25–40 s. We found that the exact time was best calculated as $\sim 1{\cdot}8 \times T$. T, a measure of the recirculation time, was estimated from the time required before the rise in the CO_2 output started to level off after the onset of

hyperventilation. In general the hypoventilation period lasted ~25 s in dogs and ~35 s in patients. It should be noted here that in the case of a left to right shunt, the shunted flow recirculates in about 10 s and will not significantly contribute to the lung perfusion value obtained with the present technique.

5 Results and discussion

Fig. 2 shows the measured time course of P_{ET} and $\dot{V}$ in a patient with a decrease in pause time corresponding to a 25% increase in minute volume. $\dot{Q}$ was measured by thermodilution to 3·6 l/min. Using this value and evaluating the slope of the CO_2 dissociation curve at $P = P_{ET}$, the time course of $P_{\bar{v}}$ can be calculated from Fick's equation and the measured P_{ET}, $\dot{V}$ data. The result, shown by the dashed line in Fig. 2, agrees with the blood gas values shown by the crosses. Plotting P_{ET} vs $\dot{V}$ in a diagram, the point (P_{ET}, $\dot{V}$) moves in time as shown in Fig. 3. Calculating the lung perfusion using the steady state point at $t = 0$ and the hyperventilation points at $t = 30$ s, 60 s, 90 s and 120 s, we get $\dot{Q} = 3{\cdot}70$, 3·55, 3·55 and 3·40 l/min, respectively.

Despite the lowering of the value with time, an effect which is due to recirculation, good agreement with the thermodilution value of 3·6 l/min is observed over a considerable time interval.

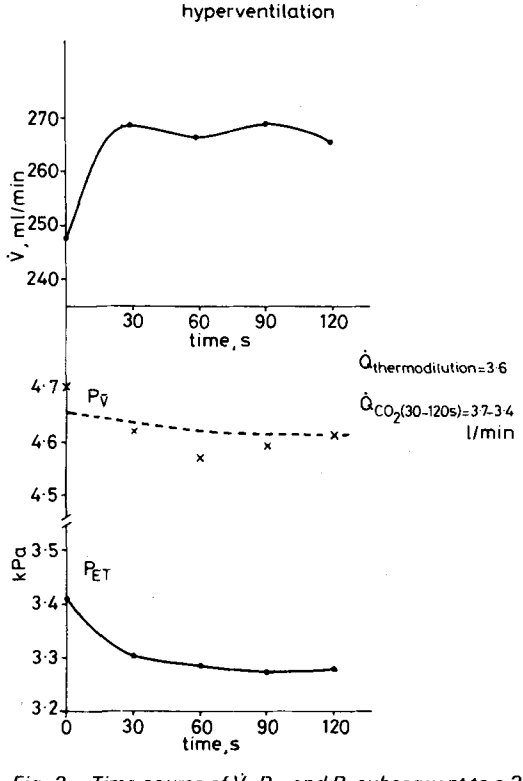

Fig. 2 Time course of $\dot{V}$, P_{ET} and $P_{\bar{v}}$ subsequent to a 25% increase in minute volume. Dashed line shows the expected course of oxygenated $P_{\bar{v}}$ as calculated from the $\dot{V}$ and P_{ET} data. Crosses represent blood gas $P_{\bar{v}}$ measurements. For a detailed discussion see the text

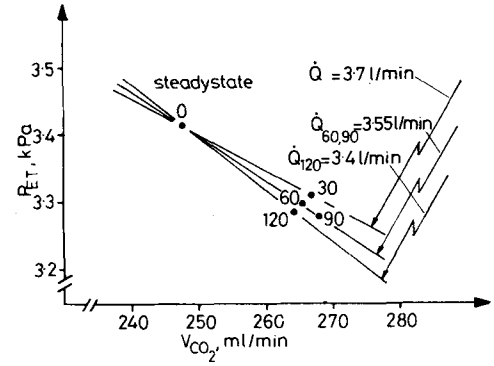

Fig. 3 P_{ET} vs $\dot{V}$ diagram showing how the point (P_{ET}, $\dot{V}$) moves in time, according to the measurements shown in Fig. 2. The $\dot{Q}$-values obtained with the steady state point and the different hyperventilation points are indicated (see also Fig. 6)

Fig. 4 shows typical tracings of P_{ET} and $\dot{V}$ when a hyperventilation setting is followed by a hypoventilation setting as described above. Note the overshoot (in the hyperventilation step) and the undershoot (in the hypoventilation step) of the CO_2 output curve. This phenomenon is in part due to the contribution from the lung tissue stores as they unload and load CO_2, respectively. The lung tissue quickly equilibrates with the new P_{ET} level (FARHI *et al.*, 1976) and, as seen in Fig. 4, will have a negligible effect on the changes in $\dot{V}$ and P_{ET} as measured at the end of the

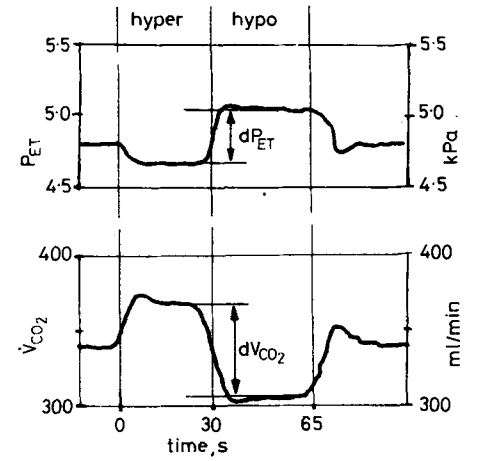

Fig. 4 Typical P_{ET} and $\dot{V}_{CO_2}$ vs time tracings for a 30 s hyperventilation period followed by a 35 s hypoventilation period. The quantities dP_{ET} and $d\dot{V}_{CO_2}$ defined in the figure yield the lung perfusion according to eqn. 10

ventilation periods. The ratio $d\dot{V}/dP_{ET}$ obtained from a tracing such as the one in Fig. 4 is, according to eqn. 10, proportional to the lung perfusion.

Fig. 5 summarises the results obtained when comparing the noninvasive CO_2 method to thermodilution determinations ($\dot{Q}_{thermo}$) of cardiac output.

We find $\dot{Q}_{CO_2} = 0{\cdot}97 \cdot \dot{Q}_{thermo}$ with a standard deviation of 18%. (Disregarding the six points obtained from a 100% increase in ventilation, the standard deviation of the material is 15%.) The standard deviation is 20% for the dogs and 8% for the patients. An individual measurement could be reproduced within 0·3 l/min.

The present method is based on three major assumptions:

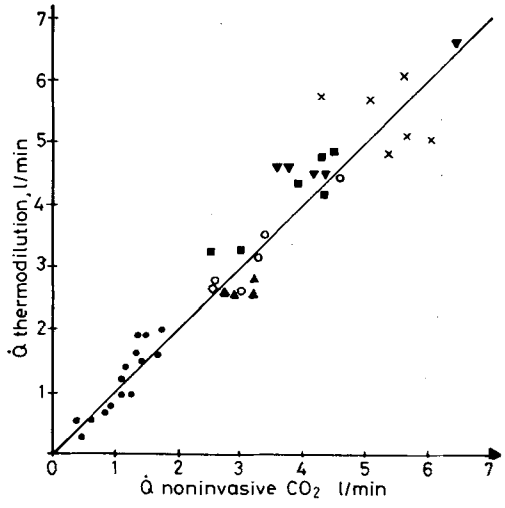

Fig. 5 Comparison between thermodilution measurements of cardiac output and the noninvasive CO_2 method. Line of identity is shown for comparison. The percentage values given below refer to the change in minute volume

Dogs:
- ▲ *steady state and 50% hyperventilation,*
- X *steady state and 100% hyperventilation,*
- ▼ *50% hyperventilation and 50% hypoventilation,*
- ■ *20% hyperventilation and 20% hypoventilation,*
- ● *20% hyperventilation and 20% hypoventilation.*

Human subjects:
- ○ *steady state and 50% hyperventilation*

(i) the patient is in steady state at the beginning of the measurement.
Since the determination of lung perfusion affects the blood gas equilibrium, steady state conditions have to be awaited between each measurement. In our experience the measurements can be repeated at an interval of ~15 min.

(ii) The changes that are induced in the CO_2 parameters P_{ET} and $\dot{V}$ must be implemented with a minimum of perturbation of the end tidal to arterial pCO_2 difference (E in eqn. 7). According to Fig. 5, the method used in this work although not necessarily the optimal one fulfills this requirement quite well.

(iii) The effect of recirculation on $P_{\bar{v}}$ is minimised for instance by a bidirectional change in ventilation, relative to the basal condition.

In addition it is important to note, when comparing results of the present method to other techniques for measuring cardiac output, that left to right shunts and anatomic right to left shunts (regions with $\dot{V}/\dot{Q} = 0$) will not be properly accounted for with the noninvasive technique.

On the other hand, since only relative changes and no accurate absolute values for the end-capillary or alveolar pCO_2 are needed in calculating the lung perfusion, it is expected that the present method is applicable to lungs in disease (the clinical validation of this claim is outside the scope of this paper). Together with the fact that the method is very simple to apply, especially in patients on mechanical ventilators, this makes our approach potentially quite attractive for clinical diagnostic purposes.

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Appendix 1

The CO_2 dissociation curve

The dissociation curve describes the relation between the CO_2 content of oxygenated blood C (in the units volume %; or ml s.t.p.d./ml) and the partial pressure of CO_2, P. The slope of the dissociation curve S is the derivative of C with respect to P. Thus, evaluated between the arterial and the mixed venous points, the slope can be obtained according to eqns. 5 and 7 as

$$S = \left(\frac{dC(P)}{dP}\right) \quad \text{for} \quad P = \frac{P_{\bar{v}} + P_{ET} + E}{2}$$

where the relation between C and P, here denoted by $C(P)$, is specified below. Since, according to eqns. 4, 6 and 7 (see also Fig. 6),

$$\frac{P_{ET1} - P_{ET2}}{\dot{V}_1 - \dot{V}_2} = \frac{P_{\bar{v}} - E - P_{ET1}}{-\dot{V}_1} \quad . \quad . \quad . \quad . \quad . \quad . \quad (12)$$

we find

$$P = \left(\frac{P_{ET1} - P_{ET2}}{\dot{V}_2 - \dot{V}_1}\right) \times \dot{V}_1 \times \tfrac{1}{2} + P_{ET1} + E \; . \; . \quad . \quad . \quad (13)$$

To derive a formula for S, the dissociation curve has to be given a mathematical form. It is easy to verify that

$$C(P) = K_1 \times \ln(1 + K_2 P) \quad . \quad . \quad . \quad . \quad . \quad . \quad (14)$$

with $K_1 = 0{\cdot}228$ and $K_2 = 1{\cdot}45$, fits an oxygenated CO_2 dissociation curve very well over a wide range. P must be expressed in the unit kPa, where

$$1\,\text{kPa} = 7{\cdot}5\,\text{mm Hg} = 10\,\text{cm}\,H_2O\,.$$

Comparing the above mathematical formula for instance to the measurements of CHRISTIANSEN, DOUGLAS and HALDANE (1914) we find less than 2 vol. % error in C everywhere from $pCO_2 = 0$ to $pCO_2 = 10$ kPa (75 mm Hg). The displacement of the dissociation curve due to various blood parameters does not constitute a major problem here since only the slope of the curve enters the calculations. The slope is a slowly changing function of P, and since the physiological range is rather limited, the function given by eqn. 14, although by no means a unique representation, is quite adequate (KLAUSEN, 1965). Calculating S according to eqn. 5 from eqn. 14 gives

$$S = \frac{K_1 \times K_2}{1 + K_2 P}$$

where P is given by eqn. 13. This gives finally

$$\frac{1}{S} = \frac{1}{K_0} + \frac{1}{K_1}\left(P_{ET1} + E - \tfrac{1}{2}\dot{V}\left(\frac{P_{ET1} - P_{ET2}}{\dot{V}_1 - \dot{V}_2}\right)\right) \quad (15)$$

where $K_0 = K_1 K_2 = 0{\cdot}332$ and $K_1 = 0{\cdot}228$.

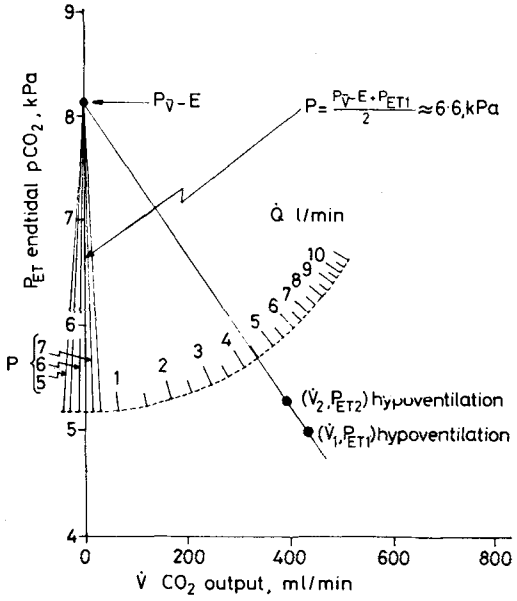

Fig. 6 End tidal pCO_2 vs CO_2 output. Simultaneously measured values of these parameters corresponding to hyper- and hypoventilation are represented by the two points. The straight line through these points intercepts the P_{ET}-axis at the value $P_{\bar{v}} - E$, where $P_{\bar{v}}$ is the mean oxygenated mixed venous CO_2 tension and E is the unknown difference between arterial and end tidal pCO_2. As explained in Appendix 2, the graduated arc is centred on the $P_{\bar{v}}$ point and the base line designated by 6·6 is aligned along the P_{ET}-axis. The straight line then indicates the pulmonary blood flow of 4·45 l/min on the scale. Since by definition (see eqn. 7) $P_{ET} = P_a - E$, the difference between the extrapolated $P_{\bar{v}} - E$ and $P_{ET} = P_a - E$ is always $P_{\bar{v}} - P_a$ irrespective of the value of E. Therefore the lung perfusion obtained is not sensitive to the precise value of E

Appendix 2

Graphical evaluation

Consider a coordinate system for end tidal pCO_2, P_{ET} vs CO_2 output $\dot{V}$ as shown in Fig. 6. The measured values $(\dot{V}_1, P_{ET1})$ and $(\dot{V}_2, P_{ET2})$ appear here as two points. The intersection of a straight line drawn through these two points with the P_{ET}-axis gives the value $P_{\bar{v}} - E$ (see eqns. 4 and 7). Now as seen from eqn. 10 the slope of the line would be proportional to the inverse of $\dot{Q}$ if the dissociation curve were linear, that is if S were a constant. The actual curvature of the dissociation curve can be taken into account to the first order by a small rotation of the line around the $P_{\bar{v}} - E$ point. In practice, a number of base lines are given on the graduated

arc. Each base line is labelled with the P-value for which the slope of the dissociation curve is evaluated. When the base line with the proper value is aligned along the P_{ET}-axis and the centre of the arc is positioned on the $P_{\bar{v}}$-point, the straight line connecting the measured points will directly indicate the pulmonary blood flow value on the scale. In the example shown in Fig. 6, $P_{ET} = 5{\cdot}0\,\text{kPa}$, $P_{\bar{v}} - E$ is extrapolated to $8{\cdot}2\,\text{kPa}$, and thus according to eqn. 5 the slope is to be taken at the mean of these two values: $P = 0{\cdot}5(8{\cdot}2 + 5{\cdot}0) = 6{\cdot}6\,\text{kPa}$. Aligning the arc so that the $P = 6{\cdot}6$ base line coincides with the P_{ET}-axis, one reads $\dot{Q} = 4{\cdot}45\,\text{l/min}$ on the scale. This is to be compared to $\dot{Q} = 4{\cdot}37\,\text{l/min}$ computed from eqn. 11. In general the accuracy of the graphical method is typically 2–3% compared to calculated values.

Also when using the graphical representation it is easy to demonstrate why the present method based on eqn. 6 is insensitive to the errors inherent in noninvasive procedures based on measurements of P_{ET}. One sees that the unknown difference E between end tidal and arterial pCO_2 also appears in the extrapolated value of the mixed venous pCO_2. Mathematically, E will cancel out when taking the arteriovenous difference; and graphically, the line in Fig. 6 will be shifted up and down as E varies, but its slope will not be changed. It is only when taking into account the curvature of the dissociation curve that a small error is introduced because of the uncertainty in the value of E.