

Clinical assessment of a rebreathing method for measuring pulmonary gas transfer

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ABSTRACT A rebreathing method for measuring carbon monoxide transfer factor (TLCO) and transfer coefficient (KCO) is evaluated. The test was performed on 42 subjects. Seventeen of these had normal lung function while the remainder suffered from various conditions, most having fibrosing alveolitis. No patients with severe airways obstruction were included in the group. The results were compared with single-breath measurements and close correlations were found between single-breath KCO and rebreathing KCO ($r = 0.78$, $p < 0.001$) and between single-breath TLCO and rebreathing TLCO ($r = 0.97$, $p < 0.001$). The reasons for discrepancies between single-breath and rebreathing values are discussed. It is concluded that measurement of rebreathing gas transfer is a useful supplement to routine tests of lung function, particularly in breathless patients with a small vital capacity.

Determining the pulmonary capacity for carbon monoxide (TLCO) and the transfer coefficient (KCO) is now a standard procedure in most pulmonary function laboratories. The single-breath method of Krogh,¹ modified by Ogilvie *et al*,² which has found wide acceptance throughout the United Kingdom, is quick, relatively easy to perform, and reproducible. It requires subjects to hold their breath for 10 seconds, however, have a vital capacity greater than 1.3 l, and be sufficiently mobile to attend the lung function laboratory. In our practice we see some patients who do not fulfil these requirements. Clark *et al*³ introduced a bedside rebreathing technique for measuring pulmonary carbon monoxide uptake, primarily intended for patients with suspected intra-alveolar haemorrhage, who are frequently too ill to undertake the single-breath test. We have applied the same method to a study of normal volunteers and patients with impaired lung function, and compared the results with those obtained by the single-breath procedure.

Methods

All subjects had measurements of forced expiratory volume in one second (FEV₁), forced vital capacity (FVC), peak expiratory flow rate (PEFR), rebreathing carbon dioxide tension (PCO₂), lung volume

(by closed-circuit helium dilution), single-breath transfer factor for carbon monoxide (TLCOSB) (with the modifications of Jones and Meade⁴), and transfer coefficient (KCO) (by the method of McGrath and Thomson⁵). Rebreathing KCO (KCORB) was measured by the method of Clark *et al*.³ A 1-litre syringe is connected via a two-way tap to a 1-litre anaesthetic bag. After the dead space has been flushed the system is filled with the helium and carbon monoxide gas mixture as in the single-breath method (about 10% He and 0.3% CO). When the gas has been thoroughly mixed and sampled, the anaesthetic bag is emptied and refilled with 0.75 l of the gas mixture from the syringe. A mouthpiece is fitted in place of the syringe and with the nose clip applied and the two-way tap open to the atmosphere the subject breathes through the system. At the end of a quiet, tidal expiration the two-way tap is turned so that the subject rebreathes from the bag, emptying it with each inhalation, at a rate of one cycle per second. The exact time for 10 cycles is recorded with a stop watch, and the bag is closed at the end of the tenth expiration. The gas inside is analysed for helium and carbon monoxide.

The rate of uptake of carbon monoxide from alveolar gas is calculated from the equation of Krogh¹:

$$KCO = \log_e \frac{F_1CO \times F_EHe}{F_ECO \times F_1He} \times \frac{23.3}{t},$$

where F_1CO = fractional carbon monoxide concentra-

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tion in the bag at the start of rebreathing; F_{ECO} = fractional carbon monoxide concentration in the bag at the end of the rebreathing period; F_{He} = fractional helium concentration in the bag at the start of rebreathing; F_{EHe} = fractional helium concentration at the end of rebreathing; t = rebreathing time in seconds. The figure 23.3 is a combined correction factor converting from millilitres to millimoles, from seconds to minutes, from fractional concentration to partial pressure of dry gas in kilopascals, and from BTPS to STPD (the latter is required because carbon monoxide uptake is expressed in millilitres or millimoles STPD by convention); it is equal to

$$\frac{1000 \times 60 \times 0.826}{22.4 \times 95.0}.$$

The units for KCO are $\text{mmol (STPD) min}^{-1} \text{ kPa}^{-1} \text{ l(BTPS)}^{-1}$ and the value is equivalent to TLCO/VA , where VA is the alveolar volume (in l(BTPS)) at which the measurement is made. VA may be calculated from the dilution of helium in the bag after rebreathing:

$$V_{\text{ABTPS}} = \frac{F_{\text{He}} \times 0.75}{F_{\text{EHe}}} \times 1.1.$$

It is equal to $V_{\text{BAG}} + V_{\text{LUNG}}$. 1.1 is an approximate ATP-to-BTPS conversion factor.

The diffusing capacity (TLCORB) may be calculated from $\text{KCORB} \times \text{VA}$, and its units are $\text{mmol(STPD) min}^{-1} \text{ kPa}^{-1}$.

The technique also allows for a measurement of the subject's functional residual capacity (FRCRB), which is the volume at which the subject starts rebreathing. It is calculated from the dilution of helium:

$$\text{FRCRB} = \frac{F_{\text{He}} \times 0.75}{F_{\text{EHe}}} - (V_{\text{B}} + V_{\text{D}}) \times 1.1,$$

where V_{B} = bag volume (0.75 l) and V_{D} = dead space volume of lung (anatomical and equipment).

These measurements were made in 17 subjects with normal lung function, two of whom were being investigated for breathlessness, and 25 with abnormal lung function (diagnoses listed in the table).

Patients with severe airways obstruction were excluded from the study because it was thought that they would be unable to rebreathe sufficiently rapidly.

Each subject rehearsed the rebreathing method before doing the test. The mean of two valid measurements of rebreathing KCO was taken from each patient.

Results

The mean results of TLCOSB, KCOSB (with their percentage of predicted normal values), TLCORB, and KCORB; FRC measured by closed-circuit helium dilution; and FRCRB for the 42 subjects are shown in the table. Values of TLCOSB ranged from 2.7 to 15.56 $\text{mmol min}^{-1} \text{ kPa}^{-1}$ and those of KCOSB from 0.64 to 2.92 $\text{mmol min}^{-1} \text{ kPa}^{-1} \text{ l}^{-1}$.

The relationship between FRC measured by closed-circuit helium dilution and FRCRB is shown in figure 1. There is a significant correlation between the values ($r = 0.75$; $p < 0.001$), though the rebreathing value (mean FRCRB = 2.96 l) is lower than the FRC measured by closed-circuit helium dilution (mean FRC = 3.27 l), particularly at larger lung volumes. The relationship between the two values is expressed by the equation

$$\text{FRCRB} = 0.092 + 0.878 \text{ FRC}.$$

The scatter diagram for KCOSB against KCORB (fig 2) shows the correlation between the measurements, which is highly significant ($r = 0.78$; $p < 0.001$). The means of the two sets of values are similar (mean KCOSB = 1.42; mean KCORB = 1.33). The relationship between the two values is given by the regression equation

$$\text{KCORB} = 1.179 \text{ KCOSB} - 0.343.$$

The highest coefficient of correlation was that between TLCOSB and TLCORB ($r = 0.97$; $p < 0.001$ —fig 3). The rebreathing transfer factor measurements (mean TLCORB = 5.29) were lower than the single-breath values (mean TLCOSB = 7.41), reflecting the fact that the rebreathing technique measures TLCO at a lower alveolar volume (effec-

Mean gas transfer measurements* in 42 patients† undergoing the rebreathing test

Age (y)	FRC closed-circuit helium dilution	FRC rebreathing	KCOSB (% predicted normal in parentheses)	KCORB	TLCOSB (% predicted normal in parentheses)	TLCORB
43-9	3.27	2.96	1.42 (82.3)	1.33	7.41 (75)	5.29

*Functional residual capacity (FRC) in lBTPS, transfer coefficient (KCO) in $\text{mmol min}^{-1} \text{ kPa}^{-1} \text{ l}^{-1}$, pulmonary diffusing capacity for carbon monoxide (TLCO) in $\text{mmol min}^{-1} \text{ kPa}^{-1}$. SB indicates the single-breath method and RB the rebreathing method.
†Twenty-six men and 16 women, suffering from asbestosis (4), asthma (1), bronchiectasis (1), bronchial carcinoma (1), bird fancier's lung (1), chronic bronchitis (1), intra-alveolar haemorrhage (2), fibrosing alveolitis (3), eosinophilic granuloma (1), mixed connective tissue disease (1), mitral valve disease (1), polyarteritis nodosa (1), scleroderma (1), sarcoidosis (4), pulmonary embolism (2) (fuller details obtainable from the authors).

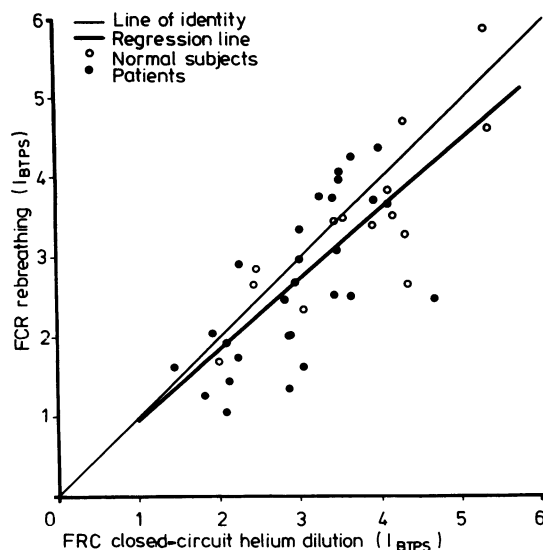


Fig 1 Relationship between functional residual capacity (FRC) measured by closed-circuit helium dilution and by the rebreathing method.

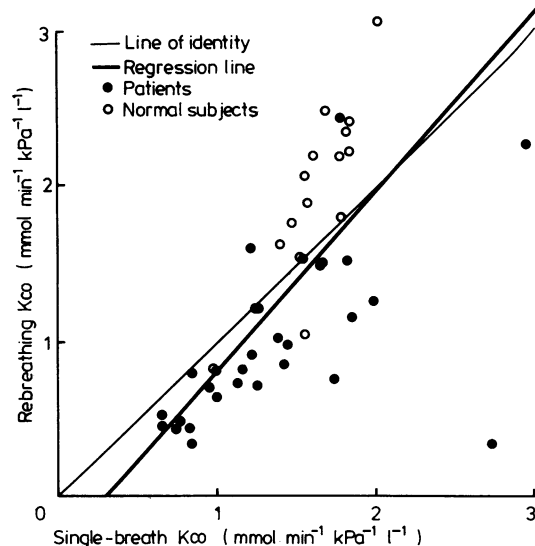


Fig 2 Relationship between the values for the transfer coefficient (KCO) obtained by the single-breath and rebreathing methods.

tively $FRC + Vb/2$) than the single-breath method (about total lung capacity). The relationship between $TLCOSB$ and $TLCORB$ is given by

$$TLCORB = 1.065 TLCOSB - 2.6.$$

The coefficients of variation for 15 duplicate

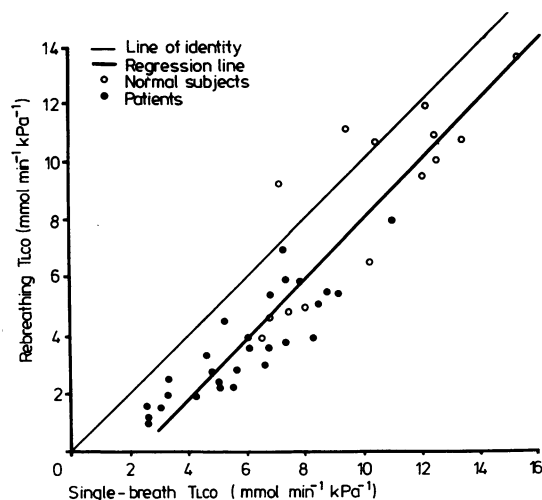


Fig 3 Relationship between the values for the pulmonary diffusing capacity for carbon monoxide ($TLCO$) obtained by the single-breath and rebreathing methods.

measurements in normal subjects were 8.7% for KCO , 9.1% for $FRCRB$, and 6.3% for $TLCORB$.

Most patients, when asked, said that they found the rebreathing method easier to perform than the single-breath method.

Discussion

The application of a rebreathing method to the measurement of pulmonary carbon monoxide uptake is not a recent innovation.⁶⁻⁸ Previous techniques, however, have suffered from drawbacks that render them impractical in the testing of breathless patients or at the bedside. The methods of Kruhoffer⁶ and Lewis *et al*⁷ require elaborate equipment which is not available in most lung function laboratories, while the method of Marshall⁸ requires a rebreathing volume of 2 l and a rebreathing time of 30 seconds—requirements that would preclude its use in severely incapacitated patients.

Several assumptions are made when Krogh's equation is applied to a rebreathing system.⁷ The first is that the mixing of carbon monoxide and helium gas mixture is instantaneous and uniform. This is assumed also in the single-breath calculation. Gas mixing would be expected to be more complete during rebreathing than in a single inhalation to total lung capacity, so this assumption is probably more valid for the rebreathing than for the single-breath technique. The fact that $FRCRB$ underestimates FRC measured by closed-circuit helium dilution indicates that 10 seconds is too short a time for the

gas to mix throughout the available lung volume when the patient is rebreathing a volume of 0.75 l. Secondly, the dead space of subject and equipment is assumed to be negligibly small. Thirdly, the time spent at end-expiration is assumed to be insignificant in relation to the time spent at full inspiration—in other words, the bag is considered an extension of the lung, and the alveolar volume for the calculation of TLCO is taken as $V_{\text{LUNG}} + V_{\text{BAG}}$. These second and third assumptions are undoubtedly false; some of the gas mixture spends some of the time exposed to surfaces which are not participating in gas exchange, so the true KCO will be underestimated. Finally, the rate of uptake of carbon monoxide is assumed to proceed exponentially from the moment rebreathing commences; this is really an extension of the first assumption. Lewis *et al*⁷ showed that in most subjects exponential decline of alveolar carbon monoxide concentration occurs only after about five seconds of rebreathing and may take longer in those with appreciable inequality of ventilation (for example, emphysema). Applying Krogh's equation to a rebreathing system therefore leads to several errors in the estimation of KCO.

There are some important differences between the rebreathing and the single-breath method. McGrath and Thompson⁵ showed that KCO varies inversely with lung volume, so that KCO at rebreathing lung volume ($FRC + V_B/2$) should be greater than the single-breath measurement (obtained at about total lung capacity). Furthermore, increased cardiac output during rebreathing and more negative intrathoracic pressure, caused by limitation of inspiration when the bag is empty, *might* lead to expansion of the pulmonary capillary blood volume and higher values of KCO. Interestingly, measurements of rebreathing KCO values in our young, healthy volunteers (recruited mostly from medical students) were generally higher than the corresponding single-breath measurements (fig 2). Possibly these normal subjects generate more effort during rebreathing than do patients with impaired lung function; this is due partly to their fitness, which facilitates rapid rebreathing, but also to their desire to impress us with their respiratory prowess. The extra effort leads to an expanded pulmonary blood volume and may account for the higher values of rebreathing KCO seen in this group.

Given all these theoretical limitations, it is surprising that KCO_{SB} agrees so closely with KCO_{RB}. KCO_{RB} cannot be taken as a measurement equivalent

to KCO_{SB}—the two values indicate the rate of uptake of pulmonary carbon monoxide at different lung volumes and under different physiological conditions. Nevertheless, the highly significant correlation between the two sets of results indicates that factors influencing the single-breath value cause a corresponding change in the rebreathing measurement. We assume that the errors in the rebreathing technique and the calculation outlined above remain fixed for all our subjects, so there is a good linear correlation between the rebreathing and the single-breath values.

We conclude that measurement of KCO and TLCO by the rebreathing method of Clark *et al*³ is a useful supplement to routine lung function tests, giving values that correlate closely with single-breath measurements. It has the advantage of simplicity (all the materials should be readily available in most lung function laboratories) and mobility (the measurement can be made at the bedside). It can be used in breathless patients with a small vital capacity and may be particularly useful for serial measurements of gas transfer in patients who become too ill to perform the single-breath test.

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