

Variability of the single-breath carbon monoxide transfer factor as a function of inspired oxygen pressure

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ABSTRACT: We measured single-breath CO transfer factor (TLCO) and alveolar oxygen partial pressure (P_{AO_2}) six times at each of three fractions of inspired oxygen (F_{IO_2}) (0.17, 0.21, 0.26) in twelve healthy subjects, to determine whether one F_{IO_2} would have the advantage of producing less variable TLCO results than the others. Measured TLCO was adjusted for the increase in carboxyhaemoglobin during the tests. We found no significant differences in intra- or interindividual variance as a function of test F_{IO_2} .

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An American Thoracic Society committee with European representation has recently standardized the single-breath carbon monoxide (CO) diffusing capacity (DLCO) or transfer factor (TLCO) [1]. The committee was divided over whether to standardize the test gas fraction of inspired oxygen (F_{IO_2}) to 0.17 as recommended by the European community or to 0.21 as is used in America. One of the primary justifications advanced for using a test gas F_{IO_2} of 0.17 is that it more closely approximates the existing oxygen concentration in the lungs thereby reducing the variability of alveolar oxygen partial pressure (P_{AO_2}) and consequently, the variability of TLCO. We tested this idea by assessing the effect of test gas F_{IO_2} on the variability of P_{AO_2} and TLCO.

Methods

Single-breath TLCO was measured six times, in twelve healthy, non-smoking subjects, at the same time of day on three different days. Test gases contained 0.3% CO, 10% helium, and one of three target oxygen concentrations (0.17, 0.21 and 0.26) (certified standard gas). Only one F_{IO_2} was used on a given day and the sequence of testing was randomized so that each subject was tested at all F_{IO_2} levels and each of the six possible sequences occurred twice.

Diffusing capacity measurements were made using an automated TLCO system (Model DS560, W.E. Collins, Braintree, MA, USA). A mass spectrometer (Perkin-Elmer 1100 medical gas analyser, Pomona, CA, USA) was used to measure oxygen fraction (F_{O_2}) in each

tank and to sample F_{O_2} and carbon dioxide fraction (F_{CO_2}) in the alveolar samples. On one test day, venepuncture was performed, before and after the sequence of six tests, to obtain haemoglobin (Hb) and carboxyhaemoglobin (COHb) concentrations.

Measurements included TLCO, alveolar volume (V_A), inspired volume (V_I), alveolar sample gas pressures (P_{AO_2} , P_{ACO_2}), Hb, and COHb. Changes in Hb and COHb during one testing session were assumed to be constant for all test sessions. Each measured TLCO was adjusted for carboxyhaemoglobin, assuming a linear increase in the measured change in COHb over the six tests [1].

Coefficients of variation (CV) and variances were calculated for each individual using the six tests at each F_{IO_2} level. Variances were compared with a paired variance ratio test [2]. To confirm earlier studies on the effect of P_{AO_2} on TLCO, we also regressed normalized TLCO values against their corresponding P_{AO_2} values [3].

Results

Summary data is presented in table 1. Mass spectrometer analysis showed the gas tanks to contain 17.5, 20.4, and 25.8% oxygen. Average V_I levels for each F_{IO_2} were 4.05, 4.09, and 4.10 l BTPS, respectively and average V_A levels were 5.66, 5.72, and 5.69 l BTPS. The average COHb increase after six tests was $3.4 \pm 0.5\%$ (SD) or 0.57% per test. There was no change in Hb. Adjustment of TLCO for carboxyhaemoglobin concentration reduced the average intraindividual CV from 3.34 to 3.02% (a 9.6% reduction). The correlation between normalized TLCO ($TLCO_{16} = 100 \times TLCO / (TLCO \text{ at}$

Table 1. - Summary data (Mean \pm SEM)

	0.175	F _{IO₂} 0.204	0.258
General data*			
PAO ₂ kPa	12.04	13.8	16.38
PACO ₂ kPa	3.68	3.76	3.76
TLCO	13.0	12.2	11.6
TLCO (adj)	13.2	12.4	11.7
Intraindividual variability**			
Average CV - PAO ₂	2.3 \pm 0.5	1.9 \pm 0.3	1.8 \pm 0.2
Average CV - TLCO (adj)	2.7 \pm 0.4	3.3 \pm 0.4	3.0 \pm 0.5
Interindividual variability***			
CV - PAO ₂	5.0	6.1	5.0
CV - TLCO (adj)	22.9	20.3	21.8

* - Averages of the mean values from the 12 subjects; ** - Average and SEM calculated from the individual coefficients of variation at each F_{IO₂}. SEM is included to indicate the variability of this statistic; *** - Calculated from the average values for each subject at each F_{IO₂}; TLCO: Single breath CO transfer factor in mmol·min⁻¹·kPa⁻¹; adj: measured value adjusted for carboxyhaemoglobin but not normalized for PAO₂; CV: coefficient of variation in percent.

a PAO₂ of 16 kPa) as described by KANNER and CRAPO [3]) and PAO₂ was:

$$TLCO_{16}(\%) = 144 - 2.72 \cdot PAO_2, r = 0.70$$

Over the PAO₂ range 10.5–17.6 kPa, TLCO fell 2.7% per kPa increase. This equation is essentially the same as that derived by KANNER and CRAPO in a different laboratory [3].

There were no significant differences in inter- or intraindividual variances for PAO₂ or in intraindividual variances for TLCO at the three F_{IO₂} levels (table 1) (p>0.05). We did not statistically compare interindividual TLCO variability as a function of F_{IO₂} because the large existing interindividual variance makes it necessary to have a prohibitively large sample size to detect even modest changes in variability. However, our average interindividual TLCO data showed no obvious differences in CV.

Discussion

Our results confirm previous reports of a 2.3–2.7% decline in TLCO with each kPa increase in PAO₂ over the narrow range of PAO₂ (10.5–17.6 kPa) commonly encountered in TLCO testing [1, 3].

The selection of a single test gas F_{IO₂} for near sea-level laboratories is important, primarily because it keeps PAO₂ within a narrower range so as to reduce

inter-laboratory variability for TLCO. Our study addressed the suggestion that decreased test variability might provide a reason to select one oxygen concentration over another. We found that, in healthy subjects, none of the studied F_{IO₂} levels had a significant advantage over the others in terms of decreased variability. Results may be different in patients with lung disease. Until more is known, the decision on test gas F_{IO₂} will have to be made arbitrarily.

References

1. Crapo RO, Gardner RM, et al. - ATS statement. Single breath carbon monoxide diffusing capacity (transfer factor). Recommendations for a standard technique. *Am Rev Respir Dis*, 1987, 136, 1299–1307.
2. Armitage P. - *In: Statistical Methods in Medical Research*. Blackwell, Oxford, 1971, pp. 165–166.
3. Kanner RE, Crapo RO. - The relationship between alveolar oxygen tension and the single-breath carbon monoxide diffusing capacity. *Am Rev Respir Dis*, 1986, 133, 676–678.

RÉSUMÉ: Nous avons mesuré la TLCO et la Po₂ d'un échantillon alvéolaire (PAO₂) à six reprises, à chacune des trois concentrations de F_{IO₂} (0.17, 0.21, 0.26) chez 12 sujets bien portants, pour déterminer si oui ou non une F_{IO₂} déterminée aurait l'avantage de produire des résultats de TLCO moins variables qu'une autre. La TLCO mesurée a été ajustée pour l'augmentation de carboxyhémoglobine durant les tests. Nous n'avons pas trouvé de différence significative de la variance intra- ou inter-individuelle en fonction de la F_{IO₂}.