Reference equations for plethysmographic lung volumes in White adults in Brazil as derived by linear regression

Thamine Lessa[1], Carlos Alberto de Castro Pereira[2], Maria Raquel Soares[2]

TO THE EDITOR:

Reference values for lung function vary according to the technique used for testing, as well as according to sample selection, sample size, and the statistical model used. In a multicenter study involving 244 never smokers and published in 2019, we derived reference equations for plethysmographic lung volumes in White adults in Brazil.[1] We used quantile regression to estimate predicted values and limits of normal, as was done in a study conducted in Germany and aimed at establishing reference values for lung volumes and airway resistance.[2] To facilitate the calculation of predicted values and limits of normal, we present here the reference equations derived by linear regression analysis.

The criteria for inclusion in the study were as follows: being over 20 years of age for females and over 25 years for males; having a BMI of 18-30 kg/m²; having no significant respiratory symptoms; having no current respiratory disease; having no history of respiratory disease; having no heart disease; having never undergone thoracic surgery; having no relevant occupational exposure history; being a never smoker; and being White (as described by the individuals themselves and as observed by the interviewer). All tests were performed by technicians or physicians certified in pulmonary function testing by the Brazilian Thoracic Association and using the same plethysmograph (Vmax Encore 22; SensorMedics, Yorba Linda, CA, USA).

In the original study,[1] quantile regression was used in order to derive reference values, whereas, in the present study, linear regression analysis was used. The same 244 White adults (122 males and 122 females) were evaluated in the two studies.

All statistical analyses were performed with the Stata statistical software package, version 12 (StataCorp LP, College Station, TX, USA) and the IBM SPSS Statistics software package, version 22.0 (IBM Corporation, Armonk, NY, USA). The median values obtained by quantile regression were compared with the mean values obtained by linear regression analysis. The mean values obtained by linear regression analysis in the present study were compared with the mean values obtained by Neder et al.[3] and those obtained by Crapo et al.[4] Paired t-tests were used for comparisons. Values of p < 0.005 were considered significant.

The linear equations and limits of normal are shown in Table 1. For males, median TLC as determined by quantile regression was 6.71 L and mean TLC as determined by linear regression analysis was 6.61 L, whereas, for females,

they were 4.78 L and 4.88 L, respectively. For males, median RV as determined by quantile regression was 4.78 L and mean RV as determined by linear regression analysis was 4.88 L, whereas, for females, they were both 1.59 L.

The differences observed in the previous study[1] were the same as those observed in the present study. For males, the differences between the mean VC and TLC values obtained by Neder et al.[3] (linear regression analysis) and those obtained by linear regression analysis in the present study were 0.51 L and 0.58 L, respectively (p < 0.001 for both). For females, they were 0.35 L and 0.20 L, respectively (p < 0.001 for both).

The differences between the predicted values obtained in the present study and those obtained by Crapo et al.[4] were irrelevant. However, the reference ranges for TLC were more sensitive in the present study because the standard error of the estimate (SEE) was smaller. For males, the SEE for TLC was 0.79 L in the study by Crapo et al.[4] and 0.61 L in the present study. Therefore, the equation presented here is more sensitive in detecting increased or decreased TLC. For females, the SEE for TLC was 0.54 L in the study by Crapo et al.[4] and 0.50 L in the present study.

Quantile regression is widely used for data analysis in non-homogeneous populations and has become a useful tool to complement the classical linear regression analysis.[5] The use of the median rather than the mean is much more robust to outliers. Another advantage is that any percentile can be estimated. However, when quantile regression is used for multiple percentiles, the curves can intersect, resulting in invalid distributions, such as the 95th percentile being less than the 90th percentile, which is impossible. Although there are methods for correcting this problem, they are very complex. Therefore, linear regression analysis is preferable when feasible. Such is the case with our sample; linear regression makes it easier to enter the equations into the software used in pulmonary function test equipment, allowing their widespread use. Therefore, the present study shows predicted values and limits of normal as determined by linear regression analysis, including means and the SEE.

We found only small differences between the mean values obtained by quantile regression and those obtained by linear regression analysis. A comparison between the values suggested by Neder et al.[3] and those presented here showed that the latter are significantly lower. They are, however, similar to those obtained by Crapo et al.[4] Nevertheless, Crapo et al.[4] found a greater dispersion of

---

1. Laboratório de Função Pulmonar, Clínica AMO – Assistência Multidisciplinar em Oncologia, Salvador (BA) Brasil.
2. Laboratório de Função Pulmonar, Centro Diagnóstico Brasil, São Paulo (SP) Brasil.

Table 1. Reference equations for plethysmographic lung volumes in White adults in Brazil as derived by linear regression. We suggest that the predicted values for RV and functional residual capacity be used without including patient weight. The limits of normal are calculated by multiplying the standard error of the estimate or residual error by 1.645 (for one-tailed variables of interest) or 1.96 (for two-tailed variables of interest).

Linear equation	Height coefficient		Age coefficient		Weight coefficient		Constant		R^2		Standard error of the estimate	
Sex[a,b]	F	M	F	M	F	M	F	M	F	M	F	M
TLC (L)	0.057	0.081	–	–	–	–	–4.205	–7.404	0.38	0.48	0.50	0.61
VC (L)	0.038	0.064	–0.016	–0.02	–	–	–1.967	–5.422	0.61	0.69	0.38	0.45
RV (L)	0.021	0.014	0.017	0.018	–	–	–2.60	–1.273	0.32	0.32	0.38	0.41
RV/TLC, %	–	–	0.345	0.305	–	–	15.58	14.723	0.50	0.53	6.1	4.7
FRC including weight	0.048	0.066	0.012	0.011	–0.018	–0.025	–4.695	–6.623	0.24	0.29	0.43	0.54
FRC without including weight	0.034	0.041	0.009	0.009	–	–	–3.381	–4.123	0.17	0.18	0.45	0.58
RV including weight	0.020	0.049	–0.006	–0.007	–0.010	–0.026	–1.462	–4.775	0.30	0.32	0.31	0.50
RV without including weight	0.012	0.023	–0.007	–0.01	–	–	–0.693	–2.16	0.26	0.18	0.32	0.55
IC (L)	0.014	0.018	–0.009	–0.011	0.013	0.020	–0.223	0.986	0.44	0.48	0.32	0.42
IC/TLC, %	–0.314	–0.360	–0.220	–0.161	0.510	0.354	89.94	91.58	0.27	0.30	6.0	5.8

F: female; M: male; FRC: functional residual capacity; and IC: inspiratory capacity. [a]Females: age, 21-92 years; height, 140-174 cm; BMI = 18.4-30.4 kg/m²; White (n = 122). [b]Males: age, 25-88 years; height, 156-189 cm; BMI = 19.7-30.1 kg/m²; White (n = 122).

TLC values, the sensitivity for detecting restrictive lung disease and mild hyperinflation therefore being lower.

In summary, reference equations for plethysmographic lung volumes in White adults in Brazil were derived by linear regression analysis in the present study. Although the values presented here are similar to those estimated by quantile regression, they are easier to use and can therefore be more widely used.

REFERENCES

1. Lessa T, Pereira CAC, Soares MR, Matos R, Guimarães VP, Sanches G, et al. Reference values for pulmonary volumes by plethysmography in a Brazilian sample of white adults. J Bras Pneumol. 2019;45(3):e20180065. https://doi.org/10.1590/1806-3713/e20180065
2. Koch B, Friedrich N, Völzke H, Jörres RA, Felix SB, Ewert R, et al. Static lung volumes and airway resistance reference values in healthy adults. Respirology. 2013;18(1):170-178. https://doi.org/10.1111/j.1440-1843.2012.02268.x
3. Neder JA, Andreoni S, Castelo-Filho A, Nery LE. Reference values for lung function tests. I. Static volumes. Braz J Med Biol Res. 1999;32(6):703-717. https://doi.org/10.1590/S0100-879X1999000600006
4. Crapo RO, Morris AH, Clayton PD, Nixon CR. Lung volumes in healthy nonsmoking adults. Bull Eur Physiopathol Respir. 1982;18(3):419-425.
5. Koenker R. Quantile Regression. Cambridge: Cambridge University Press; 2005. p. 146-147.