Short communication

Comparison of ERS’93 to the newly published GLI’17 reference values for carbon monoxide transfer factor

Ellie Oostveena, Eric Derombb, Anne-Marie Vintsb, Giuseppe Liistroc,d,∗

a Dept. of Respiratory Medicine, Antwerp University Hospital and University of Antwerp, Belgium
b Dept. of Respiratory Medicine, Ghent University Hospital, Belgium
c Université Catholique de Louvain (UCL), Institute of Experimental & Clinical Research - Pole of Pneumology, ENT and Dermatology, Brussels, Belgium
d Department of Pneumology, Cliniques Universitaires St-Luc, Brussels, Belgium

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ABSTRACT

Background: The new predicted values for the carbon monoxide transfer factor (TL,CO) for Caucasians by the Global Lung Function Initiative are available since September 2017. Several authors have previously shown that the predicted values of Cotes et al. (ERS’93), overestimated TL,CO. However, the GLI’17 authors omitted to compare their predicted values with the ERS’93 equations, still in use throughout Europe.

We present the differences between the two sets of predicted values, and in an attempt to improve the readability, used the contour plots instead of the classical 2-dimensional representations.

Methods: Predicted values were computed for males and females for ages between 18 and 70 years and heights between 155 and 180 cm using Matlab software with increments of one unit (1 yr, 1 cm).

Results: We demonstrate that GLI-‘17 predicted values of TL,CO are systematically lower than those of ERS-‘93, but also that the magnitude of the differences varies according to age, height and sex. More specifically, differences increase in both males and females by decreasing age and height, reaching up to 16% in males and 24% in females.

Conclusion: The predicted values of TL,CO by Cotes at al. are systematically larger than the new GLI’17 values. Plotting all the possible differences between predicted variables using contour graphs allows to identify the groups of subjects in whom significant changes in their predicted values will occur. Our findings should prompt physicians to investigate how switching to GLI-17 equations affects the clinical interpretation of TL,CO measurements in a real-live setting.

1. Introduction

The new predicted values of TL,CO by the working group of the Global Lung Function Initiative (GLI) [1] are available since September 2017. The GLI was undertaken since the 2005 ATS-ERS Task Force had concluded that the use of the ERS ‘93-reference values [2] are not appropriate. However, an alternative set of reference equations for spirometry for the use in European lung function laboratories was not suggested [3]. This activated Prof. Em. Quanjer in 2006 to start collecting normal data provided by authors of publications in international journals. After the publication of Stanejovic et al. on extended, complex models to describe spirometry data [4], the GLI working group was formed which became an ERS Task Force in 2010. Their final GLI collection of more than 74.000 spirometric data, resulted in an ERJ-

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Abbreviations: ERS’93, predicted values from the European Community for Steel and Coal / European Respiratory Society, published in 1993; GLI’17, predicted values from the Global Lung Function Initiative, published in 2017; TL,CO, Carbon monoxide transfer factor (diffusion capacity)

E-mail address: giuseppe.liistro@uclouvain.be (G. Liistro).

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our disappointment, the authors omitted to compare them with the ERS-’93 prediction equations [8], which are still in use throughout Europe today. For the clinician confronted with the switch from old to new reference equations, it is crucial to understand the potential clinical impact of that switch, which may eventually lead to changes in diagnostic and therapeutic cut-off values, as has recently been demonstrated when screening patients with systemic sclerosis for pulmonary hypertension and interstitial lung disease [9].

2. Methods

Conventionally, differences between two sets of reference equations are graphically expressed by plotting the function variable (i.e. TL,CO) as a function of age for a given value of height. Such a bi-dimensional representation has good readability, however, at the expense of the information contained in a three-dimensional plot, where both height and age are variables. To improve the legibility of graphs presenting differences between equations using height and age as variables, we propose to use a completely different method: the contour plot.

For the present study, the GLI ’17 predicted values of TL,CO and the GLI’17 values of lower limit of normal (LLN) were expressed as percentage of the predicted TL,CO based on the ERS-’93 equations. The computations were separately performed for males and females for ages between 18 and 80 years and heights between 155 and 190 cm with increments of one unit (1 yr, 1 cm) using Matlab software (Matlab R2014b). Each possible combination of age (n = 63) and height (n = 36) yielded variables, giving matrices of [63x36] points per sex.

3. Results

Top panels of the Fig. 1 show the conventional representation of the predicted values of TL,CO according to ERS’93 and GLI’17 as a function of age and keeping the height constant (160 cm, panel A and 190 cm, panel B). This figure shows that the GLI-’17 predicted values of TL,CO are systematically lower than those of ERS-’93, except for short males at advanced age.

The bottom panels of the figure depict the contour lines of the LLN-values of GLI ’17 expressed as percentage of the predicted ERS’93 value of TL,CO as a function of both age and height in females (C) and males (D). The shape of the lines and the non-uniform distances between these lines can be attributed to the non-linearity of the GLI-’17 equations, which contrasts with the linearity of the ERS-’93 equations. Such a
contour plot aids the clinician who still expresses the measured TLCO as %predicted of the ERS ’93 values to decide whether TLCO is abnormally low according to GLI ’17 for each combination of age and height. For instance, a measured TLCO in a 40-years-old female, 170 cm tall, of 70% predicted according to ERS ’93 (9.193 mmol/(min*kPa)* 0.70 = 6.435) is clearly above the LLN according to GLI ’17 (6.263 mmol/(min*kPa)) and thus considered as normal.

4. Conclusion

To summarize, our analysis indicates that omitting to switch to the GLI equations for TL,CO may lead to extra, unnecessary clinical research, e.g. CT scan, in young females who apparently exhibit a suspiciously low TL,CO according to ERS ’93 reference values. Future studies based on real cases could help us to assess the amount of these unnecessary tests. We thus strongly recommend that lung function laboratories in Europe change to GLI reference equations for forced expiration and transfer factor as soon as possible. With the implementation of new reference equations, all previous patient’s measurements can be recalculated to reassess the patient’s clinical status in the light of the revised normal values. In the meantime, our contour plots of the lower limit of GLI ’17 expressed relative to the ERS ’93 predicted value aids the clinicians who still use the ERS ’93 equations to decide if a measured TL,CO-value is truly abnormally low.

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References