Reference Equations for Spirometry Healthy Adult Population in Brazil

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Abstract

Background Chronic Obstructive Pulmonary Disease (COPD) is a set of diseases, has as its main characteristics a limitation of the ventilatory flow. The World Health Organization (WHO) estimates that by 2030, COPD will be the third-largest cause of death. However, for the effective diagnosis, it is necessary to use reference curves appropriate to the population in which the individual belongs, thus it is possible to identify probable limits and abnormalities.

Methods This is a cross-sectional and retrospective study conducted in a metropolitan region comprising 29 municipalities in southern Brazil. Individuals of both genders aged between 18 and 59 years, non-smokers, self-identified with white skin, participated in the study. The spirometric collections were done following the American Thoracic Society guidelines. And beyond them, mass and height were collected for determination of the Body Mass Index. The correlations between pulmonary and anthropometric variables were tested by regression analysis univariate after the selection of variables through multivariate analysis and logarithmic regression.

Results In this sample, 800 participants were evaluated, of these 533 females and 267 males. Both sexes had considerable spirometry variables values as FVC, FEV6, and FEV1, used in the development of prediction models. The only variable, with a positive correlation in both genders, was height. For the males model, the best fit variable was FVC, with R 2 = 0.417 and for females FEV, with R 2 = 0.462. Among males, was seeing a lower value for all individuals in both variables. Whereas women had similar behavior, for CVS, with slight differences in the ends of the curves, comparing FEV1, the values were higher in all evaluated.

Conclusion The prediction equations showed the previous curves were very restrictive and could be leading to false-positives. Thus, this update in the reference values would support clinical decisions on the prevention, diagnosis, and treatment of COPD.

Background

Chronic Obstructive Pulmonary Disease (COPD) is a set of diseases, has as its main characteristics a limitation of the ventilatory flow. The World Health Organization (WHO) estimates that by 2030, COPD will be the third-largest cause of death (1).

The mechanical activity of the lungs depends on their volume and distension capacity, which places the pulmonary capacity directly related to age (2), gender(3,4) ethnicity(5–7) and anthropometric factors(8) such as body mass and height. The WHO recommends that the diagnosis of these diseases be made using spirometry tests still in the basic health network (9). However, for the effective diagnosis, it is necessary to use reference curves appropriate to the population to which the individual belongs, thus it is possible to identify probable limits and abnormalities (2,10,11)

For the development of accurate reference equations, it is important to use a population similar to that in which the results will be applied, preferably with large age groups, never smokers and without a prior diagnosis of pulmonary disease (2).

This need for specificity is also repeated in countries with racial diversity, like In the United State of America, for example, there are studies with Asian(12), and Hispanic (13) populations. Another example being New Zealand, which has criteria for a population of European (14) and aboriginal origin (15). In Nigeria, the lack of studies representing the country's population led researchers to develop a study with a representative sample to providing up-to-date reference data for spirometric indices (16)

Brazil is no exception, in 2007, Pereira et al (17) published a study of spirometry predictive equations with the adult population of eight Brazilian cities, which included individuals of both sexes, white and non-smokers. In the study, the authors presented updated lung volume and capacity values for another Brazilian study conducted with the same methodology almost a decade earlier.

Brazil during its colonization process received different ethnic groups which spread across the country heterogeneously (18). In these cases, due to variability it is recommended that population groups due to geographic, ethnic, genetic and body habitus characteristics have different normal ranges of spirometry values (5). The object of the study was to generate updated values and appropriate references to the adult health population of cities in the southern region of the country.

Methods

This is a cross-sectional and retrospective study conducted in a metropolitan region comprising 29 municipalities in southern Brazil. The city of Curitiba is the coldest capital of the country and is located in the southern region of the country, being the eighth-most populous city in the country and the first in the southern region (19) The development of this region was marked by strong European colonization as occurred in most of the southern region (18). These peculiar characteristics of formation differ from the population profile found in other regions of the country. The study protocol was approved through the Plataforma Brasil system (protocol number: 39378714.5.0000.5547).

The sample was built according to the equation proposed by Barbetta, 1999 (20) considering a population of 1,893,997 inhabitants with a confidence level of 95% and an error of 4%. Individuals of both genders aged between 18 and 59 years, non-smokers, self-identified with white skin, participated in the study. All participants had their participation consented by signing an Informed Consent Form.

Individuals should not have a history of cardiorespiratory, neuromuscular disease or retinal detachment, having undergone surgery in the last year or report complaints of pain in the thoracic region, nausea and/or vomiting. Individuals who could not perform the proposed technique or had difficulty understanding any part of this research were also excluded; those who had ingested coffee, tea or alcoholic substances six hours before the procedure; those who had eaten large meals one hour before

the time specified for collection; or those who had practiced intense physical exercise thirty minutes before the time specified for evaluation.

Measurements

Anthropometrics data was collected by volunteers wearing light and barefoot clothing. The mass was measured in kilograms (kg), with the aid of a scale with a resolution of 0.1 kg, and a maximum load of 200 kg. In centimeters, by having a stadiometer attached to the scale, the height was obtained. Due to the values of mass and height, the Body Mass Index (BMI) was determined, calculated by the ratio weight/(height)^2, expressed in kg/m^2. The values classified according to the criteria of Liu et al (21).

The spirometric data were done in a reserved environment by a single certificated researcher in the use of the device, the equipment was previously installed, following the American Thoracic Society (ATS) guidelines (10) with an appropriated healthcare structure. A bidirectional spirometer (Care Fusion MicroLoop, San Diego, USA), performed the spirometry tests to ensure an accurate 10 milliliters (ml) volume and a 0.003 liters per second (l/s) ± 3% flow. The spirometry calibration equipment procedure happened following the manufacturer's recommendations.

Data analysis

Data analysis was performed using the R Core Team software (2018) R: A language and environment for statistical computing. The reference data for age, mass, height, and BMI were grouped into classes and presented accordingly to absolute (n) and relative (%) frequency. The variables descriptive analysis was calculated and presented as mean ± standard deviation.

The determination of regression equations has been according to the methodology proposed by Pereira et al (17). Correlations between the pulmonary variables Forced Vital Capacity (FVC), Forced Expiratory Volume in six seconds (FEV6) Forced Expiratory Volume in one second (FEV1) and concerning FEV1/FVC, FEV1/FEV6, and an anthropometric was tested, by univariate regression analysis. For the inclusion in the multivariate analysis, were selected variables with $p < 0.10$. For the variables as Peak Expiratory Flow (PEF), Forced Expiratory Flow after 50% of exhalation (FEF50), Forced Expiratory Flow after 75% of exhalation FEF75, the relation between FEF25-75, FEF50CVF, and FEF25-75CVF, after a univariate analysis selection a logarithmic regression happened.

However, the regression calculation obtained discrepant values detected using standardized residues between 3.3 and − 3.3 standard deviations. After the regression, the normality from each variable residue was verified graphically and through the Kolmogorov-Smirnov test with Lilliefors correction. The regression limits were calculated using the 5th percentile of the residues.

The comparison between the values predicted by the built model and the original model was through the t-student test paired. All analyses were performed separately for each sex and had a level of significance established at $p < 0.05$.

Results

Sample characteristics

In this sample, 800 participants were evaluated 533 (66.6%) females and 267 males. Table 1, presents the frequency distribution. Among men, the highest age frequency was between 18 and 23 years old and their height between 174-179 centimeters, whereas among women the most prevalent age range was between 42 and 47 years old and their height between 156 and 161 centimeters.

Table 2, represents values of position and dispersion for anthropometric and spirometry variables. Men were younger (18-23 years old) and taller (174-179 centimeters) than women, values of FEF 50% were close for both participants; males presented (3,66 l/s) and females (3,67l/s).

Both sexes had considerable spirometry variables values as FVC, FEV6, and FEV, used in the development of prediction models. Height was the only variable with a positive correlation in both genders. The values of R^2 were close between the equations, and also among the sexes. The most suitable adjustment for predicting FEV6 in females was $R^2=0.418$.

Among the variables tested for the logarithmic model only FEF 25-75 was present in the modeling for both sexes. In the developed equations, positive relationships were found only for the coefficients between spirometric variables and height. The coefficients between age and mass were negative for both sexes.

Figure 1 Shows the comparison of individuals with the expected value according to the model proposed by this study. And the estimated value projected by Pereira et al. (17) Among males, was seeing a lower value for all individuals in both variables. Whereas women had similar behavior, for CVS, with slight differences in the ends of the curves, comparing FEV1, the values were higher in all evaluated.

The comparison between the predicted values ($p<0.005$), has shown a significant difference for all the presented analyses.

In sum, the values predicted by this study varied from the previous study (17). Among men there was a reduction in predicted values for the variables tested. For FVC, the reduction was about 5% and for FEV1 around 10%, this statistically significant difference in all age groups ($p <0.05$).

The percentages achieved by the model in each variable are shown in Figure 2.

Among women, the decrease in the predicted value regarding the values of Pereira et al. (17) was less than 2% among younger women (18-23 and 24-29 years old), no statistically significant values ($p> 0.05$) were found in this comparison. Regarding FEV1 values, the predicted values increased slightly above 10% in all age groups ($p <0.05$).

Discussion

Spirometry test measures the volume of inhaled and exhaled air and shows valuable information about the cardiovascular condition of the human body. Besides, this tool is used for diagnostic and monitoring the development and evolution of diseases as well as treatments and epidemiologic survey to the public health system (9,11).

The ATS highlights two fundamental variables in the spirometric analysis, the FCV defined through the association as the maximum volume of air exhaled at the top of a forced expiry, and FEV1 as the maximum volume of exhaled air in the first-second expiration after a complete expiration (9).

There was an increase in the HRV and FEV1 values mean for both sexes in the comparison between this study and 2007’s (12).

In comparison to other populations, similar values have been found in Hispanics (13) and Asian (12) residents in the United State, to Nigerians (16), higher value appeared.

In 2007, Pereira et al. developed referenced equations for Brazil's white population (17), using linear regression models. This type of modeling demonstrated satisfactory results in developing predictive values (16,21,22). However, Brazil is a country of continental size, and great ethnic-cultural diversity. The southern region of the country has climatic and geographical characteristics diverting from the rest of the country, leading to later colonization of predominant Europeans. These factors have impacted the demographic differences and social dynamics of the region, in the same manner, it occurs in the United States and New Zealand. Consequently, using regional criteria for an accurate diagnosis is relevant. According to men's comparison of the predicted values, all individuals were classified below by Pereira et al. (17). The obstruction diagnostic differs due to the criteria, which may lead to false-positives diagnoses, resulting in possible expenditures of the public system as additional tests, and treatments avoided only with local diagnostic criteria.

FVC predicted values were among the younger women were lower than the comparative study, however, higher values were found among older women. On the other hand, the majority of FEV1 predicted values, are higher than those proposed by the author. This difference shall be related to the large presence of young women. In this study, 523 women were evaluated, 22.7% (n = 121) between 18 and 35 years old, against 19.8% (74) in accordance with previous study. The stature factor is directly related to lung capacity, in this study, the evaluated were 64.7% (n = 353) higher between 156 and 167 centimeters, whereas, in Pereira et al (12). study, most women-centered between 145 and 164 centimeters (n = 309;82.6%).

Differences in predicted values found in this study compared with 2007’s (17) were statistically significant between them. These variations were already expected as it is an update of the proposed values. The highest health organizations WHO (9), ATS (11), and European Thoracic Society (ETS) (10) recommend updating them every five years. Revisions of the values seek to correct the variations caused by changes in anthropometric pattern and lifestyle, physical activity, occupational and environmental factors (6).

Ethnicity has been one of the most influential factors of respiratory function (6). Even homogeneous populations such as China have differences between population groups including lung capacity. In a study conducted with inhabitants of the ethnic minorities, a significant difference between the groups evaluated using criteria produced for the general population was found (23).

In this sense, another point proposed in this paper is the establishment of local classification criteria in Brazil. In addition to the extensive territorial strip, the country has received populations from several locations in Africa and Europe. These ethnic groups mixed with the local indigenous population giving rise to the Brazilian population. This occupation was heterogeneous, leading to the consolidation of different population groups throughout the territory.

There are other direct and indirect factors that may influence lung capacities such as daily habits, level of physical activity, climatic factors and air quality which were not considered in this study. Another limitation is that the sample is not representative of the general population of the country, however, this limitation is necessary due to regional differences between populations. It is also suggested to conduct similar studies in other regions of the country, each one with their own classification criteria.

Conclusion

The findings of this study present an update of the predicted values for spirometry in adults, with a focus in the Brazil southern region. The prediction equations showed by previous references were very restrictive and could be leading to false-positives. Thus, this update in the reference values would support clinical decisions on the prevention, diagnosis, and treatment of pulmonary function.

Abbreviations

CODP Chronic Obstrutive Disease Pulmonary

WHO WORLD HEALTH ORGANIZATION

USA United State of America

KG kilogram

cm centimeters

BMI Body mass Index

ATS American Toraxic Association

ml militro

l/s litros por segundo

FVC Forced Vital Capacity

FEV6 Forced Expiratory Volume in six seconds

FEV1Forced Expiratory Volume in one second

PEF Pick Expiratory Flow

FEF50 Forced Expiratory Flow after 50% of exhalation

FEF75 Forced Expiratory Flow after 75% of exhalation

Declarations

Ethics Approval

The study protocol was approved through the Plataforma Brasil system (protocol

number: 39378714.5.0000.5547."

Consent to Participate

"All participants signed a free and informed consent form."

Consent to publish

"All authors declare consent to publication of manuscript"

Data

"All relevant data are within the manuscript and its Supporting Information files."

Competing interests

"The authors declare that they have no competing interests**."**

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Authors' Contributions

"MFC contributed to the data analysis, interpretation and wrote the manuscript. WLR made contributions in statistical analysis and revised the paperLU contributed to the design of the study and substantively revised the manuscript. All authors approved the final version of the manuscript.

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“Not Applicable”

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Tables

Due to technical limitations, the tables are only available as a download in the supplemental files section.

Figures

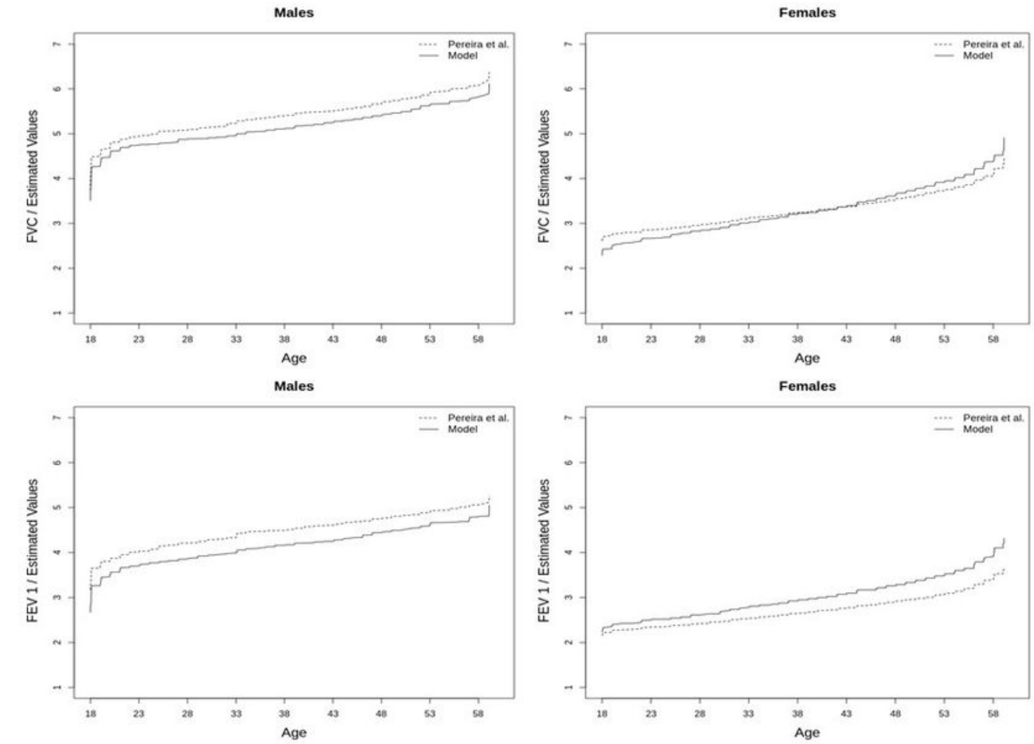

Figure 1

Comparison the values predicted by the model and Pereira et al to FVC and FEV1 for both sex

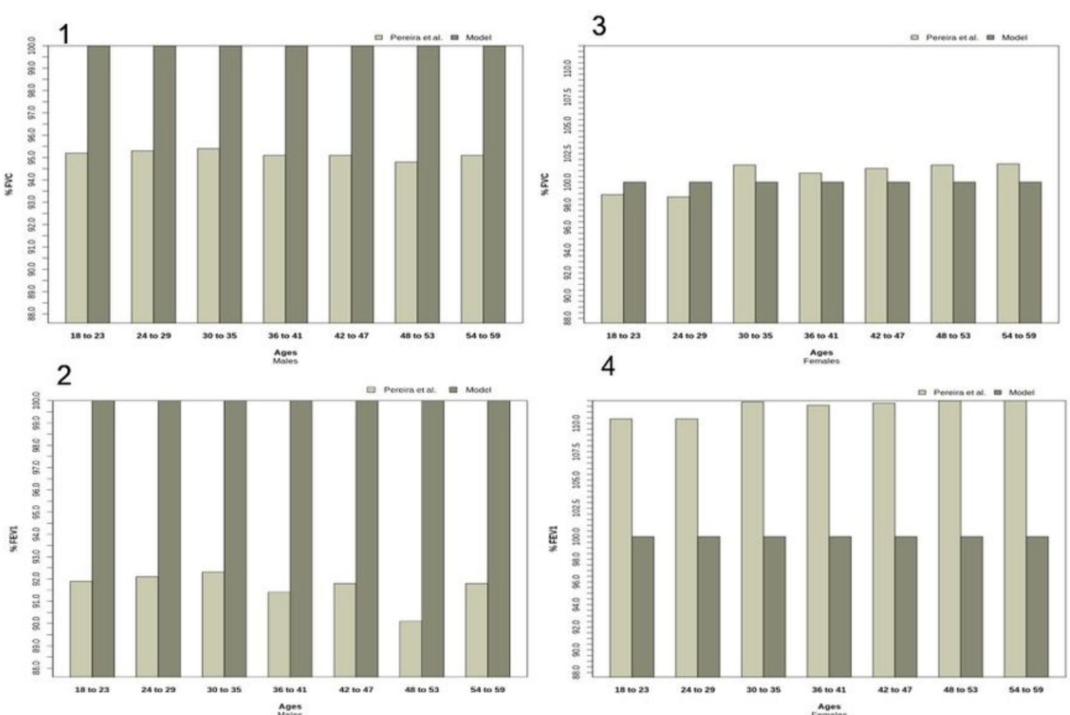

Figure 2

Percentage of the expected value achieved by the model in relation to that proposed by Pereira et al.

Supplementary Files

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- tables.xlsx