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Spirometric Reference Values for an East-African Population

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Key Words
Pulmonary function · East Africa · Reference values

Abstract
Background: Accurate interpretation of lung function testing requires appropriate reference values. Unfortunately, few African countries have produced spirometric reference values for their populations. ***Objectives:*** The present study was carried out in order to establish normal lung function values for subjects living in Rwanda, East Africa. ***Methods:*** The study was conducted in Kigali, capital of Rwanda, and in the rural district of Huye in southern Rwanda. The variables studied were forced expiratory volume in 1 s (FEV_1), forced vital capacity (FVC) and peak expiratory flow. Multiple regression analysis was performed using age, height, weight and BMI as independent variables to obtain predicted equations for both sexes. ***Results:*** Predicted equations for normal lung functions were obtained from 740 healthy nonsmoking subjects; 394 were females and 346 were males. Minor differences in FEV_1 and FVC were observed in comparison with other studies of Africans, African-Americans (difference in FEV_1 and FVC of less than 5%), Chinese and Indians. When compared with selected studies from Caucasians and white Americans, our results for FEV_1 and FVC were 9–12% and 16–18% lower in men and 12–23% and 17–28% lower in women, respectively. ***Conclusions:*** This study provides reference values for pulmonary function in a healthy, nonsmoking Rwandan population and enables comparisons to be made with other prediction equations from other populations. Spirometric reference values in our study were similar to those obtained in a study of black Americans by Hankinson et al. [Am J Crit Care Med 1999;159:179–187].

Introduction

Spirometry is an important and useful tool in the diagnosis and management of chronic pulmonary diseases. The technique is essential for assessing patients with respiratory diseases, mainly those with bronchial asthma and chronic obstructive pulmonary disease (COPD) [1]. The interpretation of pulmonary function tests is usually based on comparisons of data measured in an individual patient or subject with reference (predicted) values based on healthy subjects [2]. These references are used to identify abnormal values and, hence, the nature and degree of functional abnormality [3].

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Many different studies have established spirometric reference values for various populations but few studies have been conducted in Africa. Racial and ethnic differences in lung function have been demonstrated in previous studies and lower socioeconomic status, obesity and tobacco exposure were associated with lower lung function [4, 5].

Efforts are being made by the Global Lung Initiative task force to establish improved international lung function reference data that are representative of populations irrespective of age, ethnic group and equipment used. This will be of great importance in many areas where producing spirometric reference values is still problematic. This united approach requires data from various countries and unfortunately data from sub-Saharan Africa and most large Asian countries are lacking [6].

For an accurate interpretation of pulmonary function tests in Rwandans we conducted a study to generate appropriate reference values for the Rwandan population. The objectives of this study were to determine the spirometric reference values for healthy adult Rwandans of both sexes and to compare the results with those derived from other populations.

Methods

Study Population

The study was conducted in Kigali, the capital of Rwanda (altitude: 1,568 m), and in Huye district, a rural area located in southern Rwanda (altitude: 1,768 m). Subjects were selected from 1,824 participants from a cross-sectional study on the prevalence of asthma, atopy and COPD in Rwanda, which was conducted over 19 months between February 2008 and August 2009 [7].

There is no difference between the populations from Kigali and Huye district in terms of education and income levels in comparison with the average in Rwanda. Using information from the short version of the American Thoracic Society (ATS) questionnaire [8], only subjects who did not have respiratory problems were selected to produce the reference values. Participants who reported respiratory symptoms such as dyspnoea, chronic cough, phlegm or wheeze, those known to be asthmatic or suffering from chronic bronchitis, COPD or emphysema, pregnant women, those who reported active pulmonary tuberculosis, lung fibrosis, lung cancer or any thoracic, abdominal or recent ocular surgery were excluded from the study.

Active smokers, former smokers and subjects with obesity (BMI >30) were also excluded, the last due to the possible interference of their weight on lung function [9]. For smoking history, nonsmokers were defined as those who had never smoked or had smoked less than 100 cigarettes in their lifetime, smokers were those who currently smoked at least one cigarette per day and former smokers those who reported having smoked on a regular basis until ≥5 months before the examination. A total of 740 healthy participants aged between 18 and 80 years were finally selected to produce the reference values.

Anthropometry

Anthropometric measurements were taken using a portable stadiometer (Seca, Birmingham, UK) with a precision of 0.1 cm for the height of the subject when standing without shoes. A weighing scale (Seca) with a precision of 100 g was used for weight. BMI was calculated as weight (kg) divided by height (m) squared. We did not measure sitting height in this study.

Spirometry Measurements and Quality Control

Spirometry was performed using the same spirometer model (Microloop 3535, SPIDA, Micro Medical Ltd., UK) in 3 centers by well-trained technicians. The staff involved in the study were trained in spirometry and had passed a practical exam, and only those who showed good performance were accepted as technicians. The spirometer displayed messages to help the technician improve the subsequent quality of the readings. Calibration was checked daily with a 3-liter syringe. A senior respiratory physician supervised the 3 centers to ensure the quality of the performed tests. The results from all centers were sent daily to the Rwanda National University Hospital and spirograms for healthy participants were reviewed by a senior respiratory physician for quality control. Only tests that were technically acceptable and reproducible according to the ATS criteria [10] were considered for final analysis.

The spirometric parameters used were: forced expiratory volume in 1 s (FEV_1), forced vital capacity (FVC), FEV_1/FVC ratio and peak expiratory flow (PEF).

All spirometric measures were carried out with the subject seated, wearing a nose clip and using a disposable mouth piece. After an explanation of the procedures and a demonstration by the technician using local language, participants were asked to perform up to 8 maneuvers to obtain 3 acceptable curves for FVC. The spirometry with the largest value of FVC and FEV was considered to be the best and used for analysis. The equipment and procedures were in accordance with the ATS standards for spirometry [10].

Statistical Analysis and Generating Reference Values

Statistical analysis was done using the Statistical Package for Social Sciences version 12.0 for Windows (SPSS Inc., Chicago, Ill., USA). Sample size calculation for the initial study on the prevalence of asthma and COPD was estimated as 1,824 subjects.

Each of the spirometric variables analyzed, FEV_1, FVC, FEV_1/FVC ratio and PEF, was computed into a multiple regression model using age, height, weight and sex as predictors. Linear and nonlinear relationships were all tested during analysis to select the best model. Finally, natural logarithms and age squared were used since they improved the explained variance by 1, up to 2% compared to linear models. Lung function measurements were computed into logarithmic units and described as a function of age and height. The general form for the spirometric reference equation used in the current study was: lung function parameter: $b_0 + b_1 \ln(\text{height}) + b_2 \text{ age}^2$, where b_0 is a constant and b_1 and b_2 are coefficients for height and age respectively.

The residuals corresponding to these models did not differ significantly from a Gaussian distribution in all spirometric parameters, as determined by the Shapiro-Wilk test and the as-

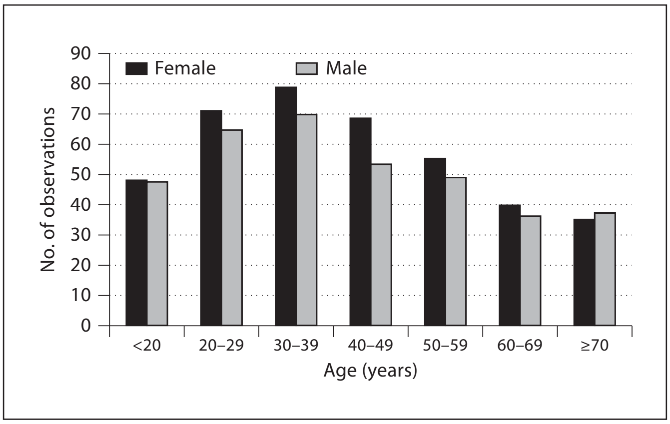

Fig. 1. Age and sex of participants.

sumptions of homoscedasticity were met. Therefore, one-sided lower 95% prediction intervals were used to determine the lower limit of normal (LLN) lung functions [11, 12].

Adult lung size is reached at 16 years of age among females [13]. The European Committee for Coal and Steel confirms the absence of change between 18 and 25 years and suggests an age of 25 years should be entered into the regression equation for the whole age range [14]. In the present study, separate equations for two age intervals (≤25 years and >25 years) did not fit the data significantly and we therefore kept a single equation.

For each spirometric equation, the fraction of explained variance (R^2) and the residual standard deviation (RSD) were determined and this allowed us to calculate the LLN which is obtained by subtracting 1.645 RSD from the predicted value squared. Predicted values were determined for each dependent variable for a subject 45 years of age with a height of 175 cm for men, and 165 cm for women.

Comparisons were performed with the χ^2 test for categorical variables and the Student t test for continuous variables. A p value of <0.05 was considered significant.

Ethical Consideration

The study was accepted by the Rwandan National Ethics Committee and the University Hospital of Ghent Ethics Committee (Belgium). The study was explained to participants in Kinyarwanda, the local language, and written informed consent was received from all the subjects as required by both ethics committees.

Results

Population Characteristics

In total 1,824 subjects were recruited for the study and among them 1,084 individuals were excluded from analysis because they did not meet the inclusion criteria. Of the remaining 740 healthy participants 346 were male and 394 were female. Table 1 shows the characteristics of the subjects who were excluded from the study: 163 (9%) were asthmatics, 589 (32.2%) had a smoking history and 108 (6%) were classified as obese with a BMI greater than 30. The age and gender distribution is illustrated in figure 1; mean age was 37 ± 11.3 years for males and 38 ± 12.5 years for females. Men and women were evenly distributed in the studied population.

Comparisons made between the populations from Kigali and Huye did not show a significant difference regarding age, height, weight, BMI or pulmonary function measurements. The anthropometric values and results for pulmonary lung function are given in table 2.

Table 1. Patients excluded from analysis

Criterion	n
Asthmatic patients	163
Diagnosis of COPD, chronic bronchitis or emphysema	85
Former smokers	286
Current smokers	304
Tuberculosis	37
Respiratory symptoms (cough, phlegm)	30
BMI >30	108
Other (various health problems)	71
Total excluded	1,084

Table 2. Characteristics of the study population (n = 740)

Characteristics	Men (n = 346)	Women (n = 394)
Age, years	37 ± 11.3	38 ± 12.5
Height, cm	169.8 ± 8.21	161.1 ± 5.2
Weight, kg	71.2 ± 10.8	59.9 ± 9.1
BMI	24.2 ± 3.3	23.1 ± 3.9
FEV_1, liters	3.21 ± 0.67	2.40 ± 0.40
FVC, liters	3.94 ± 0.50	2.78 ± 0.48
FEV_1/FVC, %	81.4 ± 5.6	86.3 ± 4.3
PEF	7.7 ± 1.55	6 ± 1.39

Data are means ± standard deviation.

Spirometric Reference Equations

Logarithmic prediction equation formula derived from men and women with age and height as independent variables are shown in table 3. Prediction equations for the means were obtained by regressing the natural logarithms of each lung parameter against ln(height) and age squared.

Table 3. Prediction equations for males and females aged between 18 and 80 years (n = 740)

	Equations	R^2	RSD
Females			
FVC	Exp $(-10.116 + 2.2238 \ln(H) - 0.000071A^2)$	0.482	0.11
FEV_1	Exp $(-8.614 + 1.905 \ln(H) - 0.0000821A^2)$	0.471	0.11
FEV_1/FVC	Exp $(5.848 + 0.268 \ln(H) - 0.000839A)$	0.621	0.08
PEF	Exp $(-5.631 + 1.416 \ln(H) + 0.00086A^2)$	0.082	0.17
Males			
FVC	Exp $(-12.528 + 2.724 \ln(H) - 0.0000564A^2)$	0.516	0.12
FEV_1	Exp $(-10.668 + 2.334 \ln(H) - 0.0000652A^2)$	0.447	0.12
FEV_1/FVC	Exp $(7.1477 - 0.518 \ln(H) - 0.001025A)$	0.073	0.06
PEF	Exp $(6.142 + 1.612 \ln(H) - 0.000216A^2)$	0.151	0.24

A = Age (years); H = height (cm); Exp(x) = e^x.

As an example, a 30-year-old man with a height of 170 cm has an FEV_1 of:

$$FEV_1 = e^{(-10.668 + 2.334 \ln(170) - (0.0000652 \times 900)} = e^{1.260} = 3.53 \text{ liters}$$

The LLN of FEV_1 is computed as:

$$\text{LLN } FEV_1 = e^{(\text{predicted} - 1.645 - \text{RSD})} = e^{1.062} = 2.89 \text{ liters}$$

While performing the regression model, age and height were found to be important independent variables for all pulmonary parameters. Weight was excluded for the prediction equations since it showed a negligible contribution compared to age and height. There was a negative correlation between FEV_1 and FVC with age (fig. 2a, b), and FEV_1 correlated positively with height (fig. 2c).

Comparison with Other Spirometric Reference Values

Comparison of our results with those from other studies is illustrated in figure 3 and 4. Equations were used to generate values of FEV_1, FVC and PEF for a male and female aged 45 years with a height of 1.75 and 1.65 m, respectively. This allowed us to make comparisons between our reference values and those from other studies of Caucasians, Africans, African-Americans, Indians and Chinese (table 4 and 5).

When we compared our findings with studies done in white populations, values for FEV_1 and FVC in the current study were lower than those derived from Caucasians with the same age and height. In men, our results for FEV_1 were 9–12% lower and FVC was 16–18% lower than those from selected studies done with white subjects. In women, FEV_1 was 12–23% lower and FVC was 17–28% lower.

Comparison with African-Americans and black Africans did not show significant differences in the pulmonary function testing values. FEV_1 and FVC in our study were similar to those for black Americans measured by Hankinson et al. [4]; when using these equations, the difference in predicted FEV_1 and FVC for subjects of the same age, sex and height was less than 5% in young ages (<40 years) and tended to increase slightly in older subjects. When compared with the study conducted in Ethiopia by Mengesha and Mekonnem [15] the difference was also small. In men, FEV_1 and FVC were 3 and 10% lower, respectively, whilst in women FEV_1 was 2% greater and FVC 8% lower.

The differences were not large when we compared our results with those from Chinese and Indian studies. In men, FEV_1 ranged from 2 to 13% greater and FVC from 2% lower to 10% greater, and in women, FEV_1 ranged from 2% lower to 12% greater and FVC from 2% lower to 14% greater. The lowest FEV_1 and FVC were observed in the study by Ashok et al. [16] of Asian Indians living in the USA. The FEV_1/FVC ratio in our study was slightly higher (for both males and females) compared to selected studies done in white subjects but the difference was not statistically significant (data not shown).

Discussion

The present study has generated a prediction equation from 740 healthy, nonsmoking Rwandan subjects. All selected participants for the generating of reference values were healthy, nonsmoking males and females without a

history of exposure to pollutants. We believe this is the first study describing the reference values for an East-African population. Spirometric data from sub-Saharan countries are lacking and we expect that data from this study will contribute to the efforts of the Global Lung Initiative to collect data from all over the world with an objective of establishing improved lung function reference values [6].

In accordance with previous studies [20, 21], a single equation for both age intervals (≤25 years and >25 years) fitted our data significantly better than two separate equations. Concerning reference values, the issue of alteration in lung function during the transition from childhood to adolescence and adulthood is an unsolved problem and needs to be studied further [22]. The European Committee for Coal and Steel considers the existence of a plateau phase between 18 and 25 years of age but this issue is controversial in the literature. Difficulties arise from the fact that in adolescence the main parameter changes (i.e. height), whereas later on height is nearly fixed and only age changes [14].

Our spirometric reference values were similar to those from other African, African-American and Asian studies. However, compared to previous studies done in Caucasian populations [4, 20], FVC and FEV_1 were lower in our subjects. Regarding the FEV_1/FVC ratio, the difference was not significant among ethnic groups. Pulmonary function test studies performed in non-European populations have shown reduced lung volumes when compared to published European reference values [4, 17, 18]. Moreover, according to the ATS statement [23], when compared with Caucasians of European descent, values for most other races usually show smaller static and dynamic lung volumes but similar or higher FEV_1/FVC %. The same statement recommends applying a correction factor of 12% when black patients are tested using spirometry reference values from studies of healthy whites. The reasons for these racial differences are not well defined. Anthropometric differences, nutritional status, socioeconomic and environment factors may explain the racial differences in pulmonary lung functions [4, 5, 12]. According to Jacobs et al. [24], differences in FEV_1 and FVC among races exist even after detailed adjustment for frame size based on sitting height, leg height, elbow breadth and biacromial diameter.

One limitation of the current study is that we did not measure sitting height. The ratio of sitting height to standing height is smaller in blacks than in whites as a result of a greater leg length and smaller thoracic size in

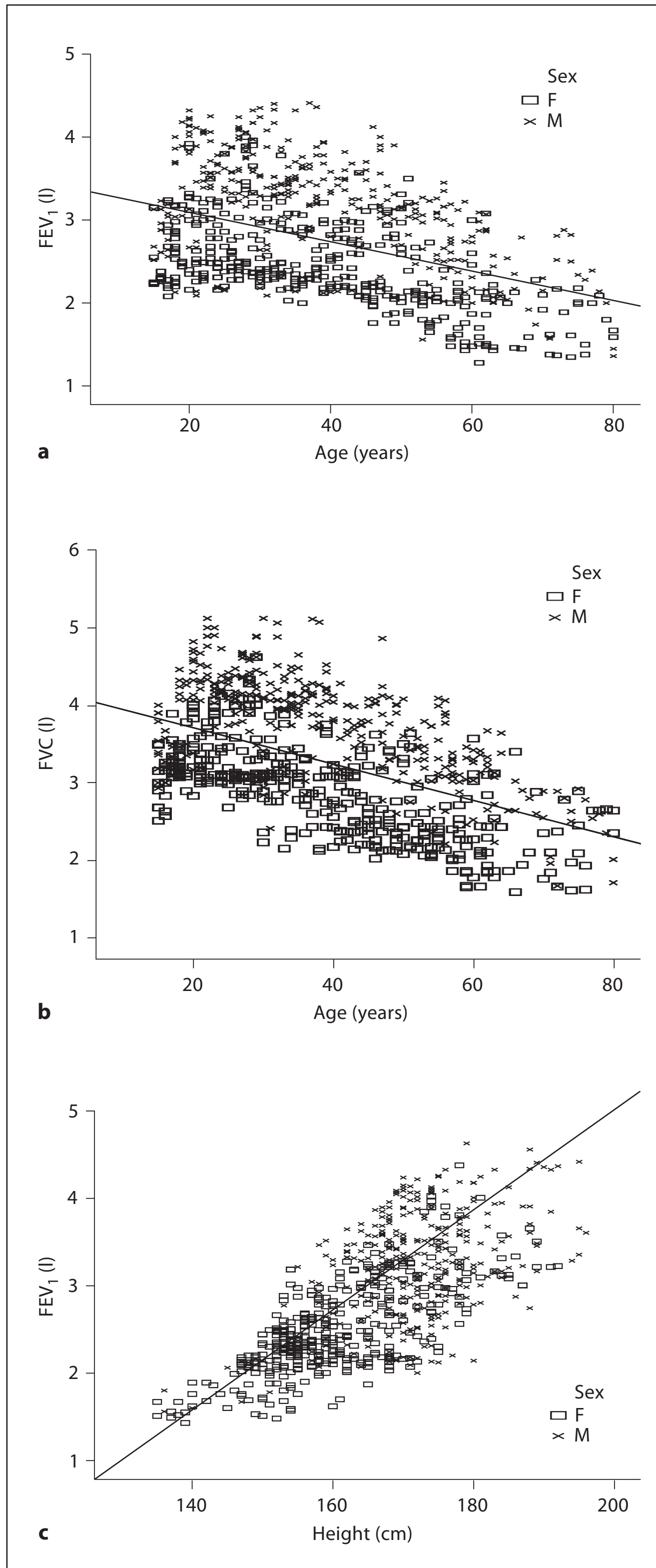

Fig. 2. Correlation between age and FEV_1 (**a**), age and FVC (**b**), and height and FEV_1 (**c**) in the studied population (males and females).

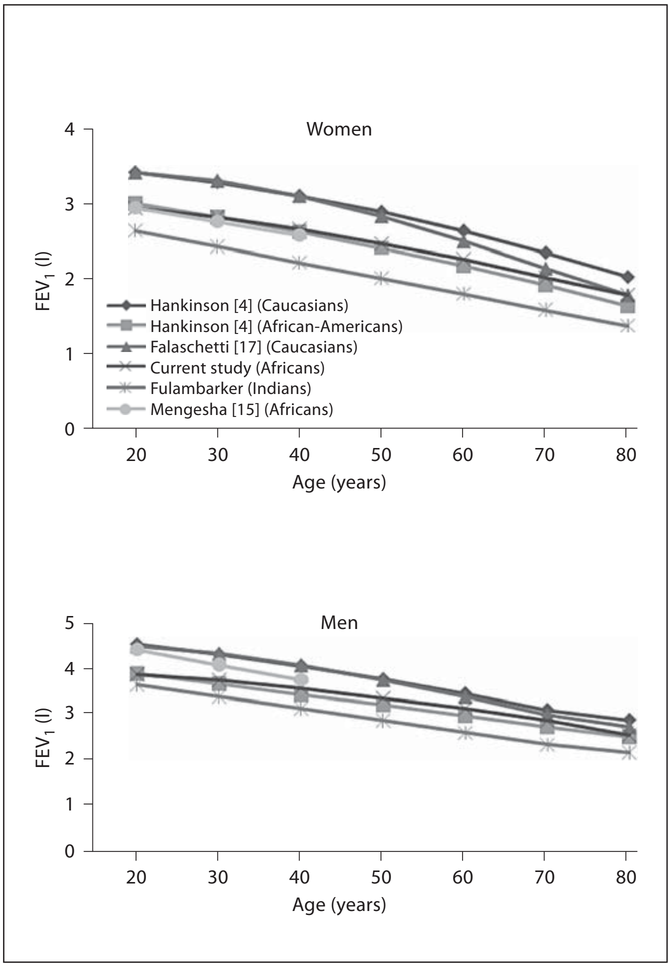

Fig. 3. Predicted FEV_1 in relation to age for males (175 cm) and females (165 cm) compared with other ethnic groups.

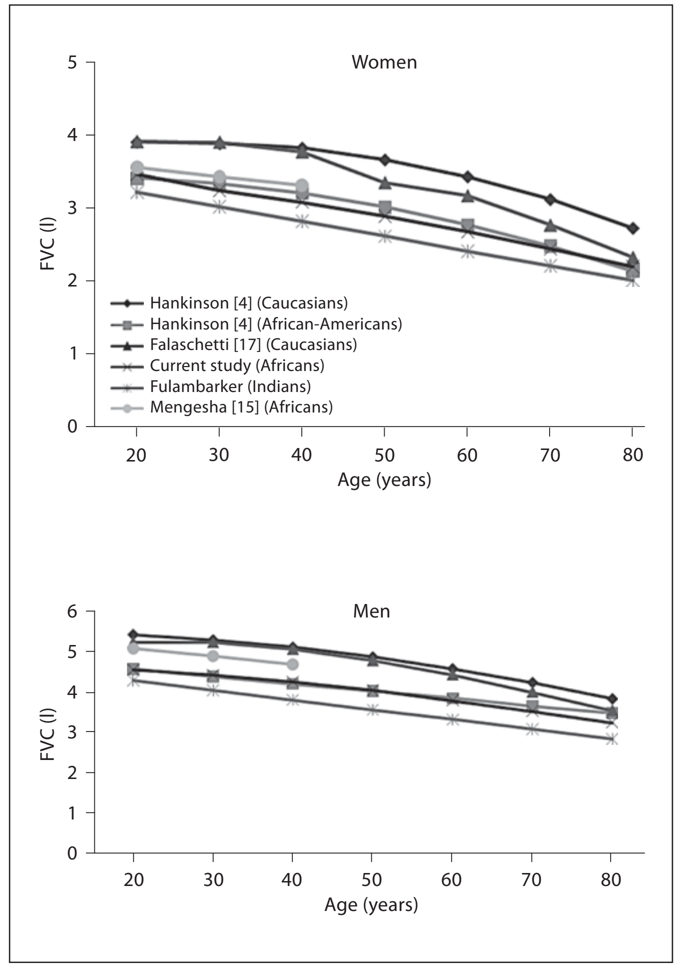

Fig. 4. Predicted FVC in relation to age for males (175 cm) and females (165 cm) compared with other ethnic groups.

blacks [25]. Also, an Iranian population was shown to have larger sitting-to-total height ratios than whites of the same age and height [26].

The reference values for spirometric lung function parameters derived from this study were similar to those calculated by Hankinson et al. [4] for African-Americans. This was not expected because we may assume there to be significant differences regarding nutrition, physical activity, air pollution and socioeconomic status between an East-African population and African Americans. Further spirometric studies with more participants are needed to assess the accuracy of using African-American equations to predict pulmonary functions in the Rwandan population.

In agreement with previous studies, we observed in our study that height was the best predictor for FEV_1, FVC and PEF [1, 4, 17, 26]. This is contrary to an African study conducted in Nigeria [27] where body weight was positively related to FVC, FEV_1 and PEF.

Weight and BMI were excluded in the present study because their contribution to the prediction equations was not significant. We believe that excluding subjects with a BMI >30 did not play a role in reducing the possible contribution of weight because they represented less than 10% of all the selected subjects.

The subjects we studied live at an altitude between 1,568 m in Kigali and 1,768 m in Huye. We did not find any significant relation between altitude and lung function. For lung volumes, no consistent differences attributable to altitude have been uncovered in studies of residents from sea level to 1,800 m [28]. Studies conducted among people living at high altitudes consistently show

Table 4. Comparison of the current study with other studies: male subjects (FEV_1 and FVC are for a 45-year-old subject with a height of 175 cm)

Authors (year)	Ethnicity	Subjects n	Age range years	FEV_1	FVC	FEV_1/ FVC
Current study	African	358	18–80	3.50	4.13	0.84
Ashok et al. [16] (2004)	Indian	226	20–80	3.02	3.69	0.81
Falaschetti et al. [17] (2004)	Caucasian	3,556	16–88	3.94	4.94	0.79
Perez-Padilla et al. [1] (2006)	Latin-American	906	>40	3.84	4.98	0.77
Pereira et al. [18] (2007)	White	270	26–86	3.99	4.93	0.80
Ip et al. [19] (2006)	Chinese	494	19–80	3.41	4.21	0.81
Hankinson et al. [4] (1999)	Caucasian	898	8–80	3.95	5.02	0.77
Hankinson et al. [4] (1999)	African-American	898	8–80	3.34	4.12	0.82
Mengesha and Mekonnem [15] (1985)	African	260	18–47	3.61	4.60	0.78

Table 5. Comparison of the current study with other studies: female subjects (FEV_1 and FVC are for a 45-year-old subject with a height of 165 cm)

Authors (year)	Ethnicity	Subjects n	Age range years	FEV_1	FVC	FEV_1/ FVC
Current study	African	392	18–80	2.55	2.97	0.85
Ashok et al. [16] (2004)	Indian	137	20–80	2.12	2.55	0.83
Falaschetti et al. [17] (2004)	Caucasian	2,497	16–88	3.32	4.13	0.80
Perez-Padilla et al. [1] (2006)	Latin-American	635	>40	2.86	3.63	0.78
Pereira et al. [18] (2007)	White	373	26–86	2.91	3.58	0.81
Ip et al. [19] (2006)	Chinese	594	19–80	2.49	3.05	0.82
Hankinson et al. [4] (1999)	Caucasian	594	8–80	3.01	3.75	0.80
Hankinson et al. [4] (1999)	African-American	1,383	8–80	2.53	3.10	0.81
Mengesha and Mekonnem [15] (1985)	African	260	18–47	2.50	3.24	0.77

higher spirometric values as a result of adaptation to chronic hypoxia and high levels of habitual exercise. The increase in lung volume varies depending on when acclimatization occurred and the duration of exposure to high altitude [29].

Conclusion

This present study shows significant differences in pulmonary function values between Africans and other populations, and therefore confirms the necessity for races and ethnic groups to have their own reference values. Spirometric reference values in our study were similar to those for black Americans recorded by Hankinson et al. [4]. Considering the similarities between inhabitants of the African Great Lakes region, the reference equations obtained in this Rwandan population can be used in neighbouring countries while waiting for further studies to be conducted in the region.

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Financial Disclosure and Conflicts of Interest

All authors report no conflict of interest and have agreed to the publication of this study, to which they all contributed.

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