Lung
DOI 10.1007/s00408-009-9148-4

Normal Spirometric Reference Values for Omani Adults

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Received: 18 November 2008 / Accepted: 29 March 2009

Abstract International guidelines recommend the use of population-specific reference values to eliminate the well-recognized influence of ethnic variation on lung function. This study was designed to derive spirometric prediction equations for healthy Omani adults. Forced vital capacity (FVC), forced expiratory volume in one second (FEV_1), peak expiratory flow rate (PEFR), and forced expiratory flow at 25% to 75% of FVC ($FEF_{25-75\%}$) were measured in 419 "healthy" nonsmoking Omani adults (256 men, 163 women), aged 18–65 years. Multiple linear regression analysis was performed for each spirometric parameter against age, height, and weight for men and women separately, and prediction equations for all the above parameters were derived and compared with values derived using equations published from other populations. All measured spirometric parameters increased with height and decreased with age, and they were all significantly higher in men. In contrast, FEV_1/FVC% values decreased with height and increased with age and were higher in women. The predicted normal values of FVC and FEV_1 for our subjects using the derived equations were lower by 7–17% compared with respective Caucasian values, with smaller difference in the predicted values of PEFR, FEV_1/FVC%, and $FEF_{25-75\%}$. This report presents previously unavailable spirometric reference equations for the Omani adults. Our findings highlight the need to use reference values based on updated data derived from relevant populations.

Keywords Lung function · Spirometry · Reference values · Ethnic Arab · Omani

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Introduction

Spirometry is a widely used basic lung function test that is increasingly advocated for use in the screening, diagnosis, and monitoring of respiratory diseases [1]. The interpretation and categorization of spirometric results depend on comparison with reference values derived from "normal" populations [2]. Hence, the accuracy of the reference values has important implications for patients, health-care providers, and researchers [3].

Most pulmonary function laboratories use reference values derived from western populations [1, 4]. However, many studies have demonstrated that significant ethnic differences exist in normal pulmonary function values and prediction equations based on western populations may not be accurate for others [1, 5, 6]. In general, equations developed for Caucasians significantly overestimate predicted normal reference lung function values in other populations [5–7].

Because failure to account for ethnic differences in lung function when they exist could lead to errors in diagnosis and classification of lung function impairment, international guidelines recommend the use of population-specific

Published online: 28 April 2009

reference equations [1, 4, 8]. It is further recommended to use recently developed equations to ensure compliance with the current international guidelines and to reduce the environmental influences between generations within the same population [1]. However, only limited data are available on normal prediction equations for spirometry in Arabs [1, 9–14]. Moreover, all of the available studies were reported during the 1980s, thus predating the recent international guidelines for standardization of lung function equipment and measurement procedures. Lung function laboratories in Oman, and perhaps in other Arab countries, are using prediction equations based on western populations with adjustment factors for non-Caucasians. These adjustment factors were based on comparison with other ethnic groups, mainly Indian, Chinese, and black Americans, and have not been validated in Arabs [1]. Hence, the development of new lung function reference values for Arab communities becomes essential. This study was designed to derive spirometric prediction equations for healthy Omani adults and to compare their predicted values with those from other populations.

Patients and Methods

In this cross-sectional study, the reference population sample, men and women aged 18 years and older, was obtained by inviting visitors to the Sultan Qaboos University Hospital (SQUH) booth in a commercial exhibition center during the annual fair (Muscat Festival), as well as the healthy relatives accompanying patients to our hospital, SQUH to participate in the study. All subjects were invited to have their lung function checked, at the same time explaining to them the purpose of the study. The Muscat Festival coincides with school holidays in January and attracts visitors from all over Oman. In addition, SQUH is a tertiary care hospital and receives patients from all over the country.

With the help of the research team, all the volunteers completed an Arabic version of the European Respiratory Health Survey Questionnaire [15]. Thus smokers, persons with respiratory or cardiac problems, and persons with a recent respiratory infection were excluded. Obese persons (BMI > 35 kg/m^2) also were excluded. A total of 561 (354 men) subjects completed the respiratory questionnaires and performed spirometry. The project was approved by the ethics committee of the Sultan Qaboos University and consent was obtained from all participants before collecting the data.

Measurements

Standing height to the nearest centimeter without shoes and weight to the nearest kilogram were measured. Manual height and weight scale was used and was calibrated daily. Age was recorded as completed years. Spirometry was performed using the same portable spirometer (Compaq, Buckingham, UK) and all measurements were performed by two trained technicians, in accordance with the American Thoracic Society guidelines [4]. The spirometer was checked for leaks and calibrated at the start of the day and recalibrated after every six subjects. Tests were performed with subjects in a sitting position. For measurements of vital capacity (VC), subjects were asked to take in a maximum breath and blow out through the mouth, with the nose clipped, into the spirometer at a steady rate to their maximum expiration. For measurements of forced vital capacity (FVC), they were asked to blow out as fast and as long as possible. A minimum of three to a maximum of five trials were performed for each maneuver. The values of the expiratory flow rate (PEFR) and forced expiratory volume in the first second (FEV_1) were obtained from the FVC maneuver, and FEV_1 as a percentage of FVC (FEV_1/FVC) was calculated. All spirograms were assessed for technical acceptability using standard objective criteria [4] (smooth and continuous curve, apparent maximal effort, good start and no evidence of false start, excessive hesitation, coughing, early termination, leaks, or obstructive mouthpiece). The FVC and FEV_1 values from the best two tracings were within 5% of each other. The largest values from acceptable tests were reported for each lung function parameter.

Statistical Analysis

Linear regression equations for each of the spirometric parameters on age, height, and weight were computed, taken alone and then together by applying stepwise multivariant analysis. The analysis was repeated on logarithmic transformation of different variables to choose models with the best fit. The coefficient of determination (R^2) and the regression coefficient values for each lung function parameter were derived. For all indices, simple linear models provided an acceptable fit to the data, and therefore, linear models were chosen as the basic format for evaluating the relationships between the lung function parameters as the dependent variables and age, height, and weight as the independent variables. Correlation coefficient among the spirometric parameters for age, height, and weight for each sex also were derived separately. The predicted lower limit of normal (LLN) for each lung function parameter was calculated by subtracting 1.64 times the residual standard deviation (RSD) from the predicted mean reference value [1].

The predicted, percent predicted, and lower limit of normal for our subjects for each of the lung function parameters derived using the prediction equations of the present study were compared with four sets of different published prediction equations: one from an Arabian population (Jordanian) [9], one from a neighboring developing country (Pakistan) [16], and the two others from the widely used western standards—the U.S. National Health and Nutrition Examination Survey (NHANES III), and the European Community for Coal and Steel (ECCS) reference equations [5, 8]. In addition, the prediction equation for $FEV_1/FVC\%$ in our study was compared with the "universal" race-independent equation proposed by Hansen and colleagues: ($FEV_1/FVC\%$ for both genders = 98.8 − 0.25 * age − 1.79 * measured FVC) [17]. Comparison between measured values of lung function parameters and their respective predicted values by different equations were performed using the paired-sample Student *t*-test. A P value < 0.05 was considered significant.

Results

From the total sample of 561 subjects, 142 (98 men and 44 women) were excluded on the basis of: history of current or ex-smoking ($n = 55$), respiratory symptoms ($n = 40$), BMI > 35 kg/m^2 ($n = 15$), and unacceptable spirometry ($n = 32$). The remaining 419 subjects (74.7% of the original sample: 256 men: mean age and height, 32.6 ± 10.5 years and 167.5 ± 6.3 cm; and 163 women: mean age and height, 33 ± 12.3 years and 155.2 ± 6.2 cm) were included in the analysis. Table 1 shows the characteristics and age group distribution of the final study sample.

All measured lung function variables (VC, FVC, FEV_1, PEFR, and $FEF_{25–75\%}$) correlated positively with height and negatively with age. The highest correlation for height occurred with FVC ($r = 0.54$ and 0.55 for men and women, respectively; $P < 0.001$) and FEV_1 ($r = 0.48$ for males and 0.53 for females; $P < 0.001$), and the lowest correlation occurred with $FEF_{25–75\%}$ ($r = 0.14$ for males and 0.21 for females; $P < 0.001$). For age, the highest correlation was with FEV_1 ($r = -0.49$ for men and $r = -0.47$ for women, $P < 0.001$) and the lowest correlation was with PEFR ($r = -0.24$ for men, $P < 0.001$, and $r = 0.17$ for women, $P = 0.03$). In contrast, the correlations of $FEV_1/FVC\%$ with height and age were weak ($r = -0.15$ for height in men, $P = 0.01$, and $r = 0.22$ for age in women, $P = 0.01$) or not statistically significant ($r = -0.01$ for height in women, $P = 0.92$ and $r = -0.03$ for age in men, $P = 0.69$).

In the regression model, age and height were found to be important independent variables for all pulmonary function parameters. The addition of weight to the regression models did not offer any additional significant improvement in the models fit as indicated by the R^2 values. Therefore, only age and height were used in the reference equations for all lung function parameters. Table 2 shows the results of regression analysis for lung function parameters (VC, FVC, FEV_1, FEV_1/FVC %, PEFR, and $FEF_{25–75}$) for both sexes. Each lung function value can be estimated by using the following equation: $y = a * age + b * height\ (cm) + c$: where y is the mean predicted lung function value, and a, b, and c are the regression coefficients for age in years, height in centimeters, and the constant, respectively. The predicted lower limit of normal (LLN) for each lung function parameter can be calculated by subtracting the figure in the last column (1.64 * RSD) from the mean predicted value.

Table 3 compares the mean predicted and percent predicted values of lung function parameters of our subjects derived using our equations with the values for the same parameters derived using the selected prediction equations. It also shows the percentage of our subjects found to have values below the lower limit of normal when each of these prediction equations were used. The mean measured FVC and FEV_1 and PEFR values were significantly lower than their predicted values by the European and American equations in both men and women. These differences resulted in classifying a large proportion of our normal subject as below the predicted lower limit of normality by these equations. In contrast, the mean measured $FEV_1/FVC\%$ was significantly higher than their predicted values using the European and American equations.

The mean predicted values of FVC and FEV_1 calculated by using the Jordanian equation were higher than the corresponding Caucasian predictions resulting in percent predicted value for our subjects settling in the range of 80–85%. In contrast, all measured values in our subjects except FEV1 in women were significantly higher than their predicted values when the equations from Pakistan were used. Among all these equations tested, the values using the Pakistani one were closer to our predicted values as well as

Table 1 Demographic characteristics presented as mean (SD) and age group distribution of the study subjects ($n = 419$)

	Men (256)	Women (163)
Age (years)	32.6 (10.5)	33.0 (12.3)
Height (cm)	167.5 (6.3)	155.2 (6.1)
Weight (kg)	71.3 (11.8)	62.2 (11.6)
BMI (kg/m^2)	25.4 (4)	26.0 (4.6)
Age groups (mean age, years)		
18–25	76 (22.7)	53 (21.5)
26–35	94 (29.7)	54 (29.2)
35–45	54 (39.5)	28 (49.6)
46–55	19 (50.4)	17 (49.9)
56–65	13 (59.1)	11 (61.6)

Table 2 Regression coefficients and constants of the prediction equations of ventilatory flows derived from 419 healthy Omani adults (aged 18–65 years)

Variable	Age (years)	Height (cm)	Constant	R^2	RSD	1.64 * RSD
Men						
VC (l/min)	−0.024	0.048	−3.19	0.5	0.41	0.67
FVC (l/min)	−0.024	0.046	−2.97	0.48	0.41	0.67
FEV_1 (l/min)	−0.021	0.034	−1.68	0.44	0.37	0.61
FEV_1/FVC (%)	−0.017	−0.123	105.21	0.02	4.98	8.17
PEF (l/s)	−0.031	0.069	−1.87	0.15	1.35	2.21
$FEF_{25-75\%}$ (l/s)	−0.033	0.017	2.32	0.17	0.83	1.36
Women						
VC (l/min)	−0.016	0.043	−3.27	0.46	0.38	0.62
FVC (l/min)	−0.016	0.043	−3.24	0.46	0.36	0.59
FEV_1 (l/min)	−0.016	0.037	−2.68	0.47	0.32	0.52
FEV_1/FVC (%)	−0.075	−0.014	90.51	0.05	4.11	6.74
PEF (l/s)	−0.013	0.075	−4.83	0.22	0.94	1.54
$FEF_{25-75\%}$ (l/s)	−0.023	0.025	0.31	0.20	0.67	1.1

FVC forced vital capacity, *FEV_1* forced expiratory volume in one second, *PEF* peak expiratory flow, *$FEF_{25-75\%}$* forced mid-expiratory flow. *RSD* is the standard deviation of the residuals (residuals = observed − predicted) and the value of 1.64 * RSD corresponds to the prediction value at the lower fifth percentile. The lower limit of normal for each parameter can be calculated by subtracting 1.64 * RSD from the predicted mean

Predicted lung function $= a * age + b * height\ (cm) + c$

the measured values in our subjects with the differences ranging from 0–11%.

When the race independent equation for the prediction of FEV1/FVC was compared with the predicted values by our equations (Fig. 1), a slight but statistically significant difference was noticed (84.6 vs. 83.8, $P < 0.001$ for men, and 85.9 vs. 85.4, $P = 0.001$ for women). However, the difference between the means of the measured values of our subjects and the corresponding predicted values by our equations was not significant ($P = 0.16$ for men and 0.95 for women). The difference between our measured values and the predicted values using the Hansen equation also was not significant ($P = 0.39$ for men and 0.17 for women).

Discussion

The availability of valid reference values is a key issue in the evaluation of lung function in individuals [2]. We have recently developed reference spirometric equations for Omani children, which showed that the predicted normal values of Omani children were 5–10% lower than respective Caucasian values [18]. In the present study, we generated normal spirometric reference values from 419 healthy, nonsmoking Omani adults. This is the first report on spirometric reference values in Omani adults and the only report form an Arab population in the last two decades.

Among the only six studies on the reference values form the Arab populations, four were limited to men or women [9–14]. Like most old studies on lung function reference values, these reports have limited validity for current use because the equipment, technique, and procedures were not standardized with current international guidelines [1, 4].

The associations of measured lung function parameters (VC, FVC, FEV_1, PEFR, and $FEF_{25-75\%}$) with age and height found in our study, including the higher values in men, were similar to results from other populations [1]. The association of the calculated FEV_1/FVC% with sex, age, and height also were consistent with findings in other populations [1]. In our subjects, the correlations of FEV_1/FVC% with age and height were weak and had different directions in men and women. In addition, the mean FEV_1/FVC values in women were slightly higher than men. Studies using the same equipment and techniques to examine several ethnic groups have shown higher values for FEV_1/FVC% in non-Caucasians and also in women in general [5, 6]. Moreover, it was recently shown by Hansen et al. that only age and the measured FVC were dominant factors in determining normal FEV_1/FVC% and that these two factors, rather than the usual ones (age, height, sex, and ethnicity), are adequate to predict the mean and normal limits [17]. This is not unexpected because height, sex, and ethnicity have already been accounted for in the FVC absolute values. In our study, we found no significant difference between the predicted FEV_1/FVC% values of our subjects derived by our new gender- and population-

Table 3 Mean ventilatory parameters of our population (256 men and 163 women) with comparisons between predicted values obtained by predicted equations of the present study and the selected equations from the literature

	Mean (SD) predicted values					
	Observed	Present study	Jordanean[9]	Pakistanis[16]	ECSC[8]	NHANES III[5]
Men						
No. of subject	256	256	144	321	Pooled data	476
Age range (years)	18–65	18–65	20–60	15–65	18–70	21–80
FVC (L)	3.96 (0.57)	3.95 (0.4)	4.92* (0.46)	3.86* (0.3)	4.46* (0.47)	4.74* (0.36)
% predicted		100.4 (10.4)	80.4 (8.4)	102.6 (10.9)	89 (10.2)	83.5 (9.2)
% of subjects below LLN		2.3	56.3	0	10.2	45.5
FEV_1 (L)	3.32 (0.47)	3.33 (0.33)	4.12 (0.45)	3.03* (0.29)	3.76* (0.42)	3.88* (0.04)
% predicted		99.9 (10.7)	80.8 (8.8)	109.6 (12.2)	88.6 (9.7)	85.8 (9.4)
% of subject below LLN		3.5	53.1	0	12.9	35.5
FEV_1/FVC%	84.1 (5)	84.6 (0.8)	–	–	81.3* (1.9)	81.3* (2.2)
% predicted		99.5 (5.9)	–	–	103.5 (6.6)	103 (6.7)
% of subjects below LLN		5.5	–	–	0	1.2
PEFR (L/s)	8.67 (1.45)	8.67 (0.56)	–	7.89* (0.63)	9.03* (0.61)	9.55* (0.55)
% predicted		100.0 (15.5)	–	109.9 (17.6)	96.1 (14.9)	90.8 (14.5)
% of subjects below LLN		2	–	0	7	16.8
$FEF_{25–75}$ (L/s)	3.99 (0.91)	4.09 (0.37)	3.84* (0.48)	3.67* (0.35)	4.54* (0.48)	3.87* (0.58)
% predicted		97.6 (19.9)	104.4 (22.2)	109.0 (22.4)	88.0 (17.7)	103.1 (21.7)
% of subjects below LLN		5.1	0	0	7.0	2.7
Women						
No. of subjects	163	163	117	183	Pooled data	927
Age range (years)	18–65	18–65	20–60	15–65	18–70	21–80
FVC (L)	2.90 (0.50)	2.91 (0.34)	3.51* (0.36)	2.79* (0.37)	3.13* (0.43)	3.36* (0.33)
% predicted		99.8 (12.5)	82.5 (10.4)	104.3 (13.3)	93.1 (12.2)	86.1 (11.1)
% of subjects below LLN		2.4%	38.7	0	9.2	35.0
FEV_1 (L)	2.49 (0.44)	2.49 (0.31)	2.93* (0.35)	2.47	2.71* (0.40)	2.85* (0.33)
% predicted		100.1 (12.9)	85.0 (11.3)	100.7 (13.2)	92.5 (12.6)	87.4 (11.4)
% of subjects below LLN		3.1	23.9	0	11.0	28.2
FEV_1/FVC%	85.8 (4.2)	85.9 (0.9)	–	–	82.8* (2.3)	83.8* (2.6)
% predicted		99.8 (4.8)	–	–	103.7 (5.3)	102 (5.4)
% of subjects below LLN		4.3	–	–	0	0.6
PEFR (L/s)	6.31 (1.06)	6.38 (0.49)	–	6.48* (0.67)	6.44* (0.5)	6.43* (0.43)
% predicted		98.9 (14.6)	–	97.4 (14.8)	98.2 (14.8)	98.0 (13.9)
% of subjects below LLN		2.5	–	0	5.5	4.3
$FEF_{25–75}$ (L/s)	3.39 (0.74)	3.43 (0.33)	3.13* (0.47)	3.16* (0.38)	3.74* (0.43)	3.17* (0.45)
% predicted		99.0 (19.1)	108.3 (22.9)	107.3 (22.7)	91.1 (16.8)	106.9 (21.1)
% of subjects below LLN		4.3	0	0	6.1	2.5

specific equation or by this race- and gender-independent equation. We support the use of this universal equation for the prediction of FEV_1/FVC% when population-specific equation for these parameters is not available [17].

The ethnic variation in lung function is well documented [1, 7]. FVC and FEV_1 in Caucasians have been consistently found to be larger than other ethnic groups, including Asian, Africans and American blacks, and Hispanics [5–7]. Several factors have been proposed to explain the ethnic variation in lung function [5, 19–23]. Genetic factors may control body shape and lung function development and decline with age. For example, Caucasians tend to have larger trunk-to-leg ratio at a given height, leading to larger vital capacity compared with blacks. Factors, such as nutrition, exercise, air quality, occupational exposures, and smoking, also may affect lung function. These factors vary among individuals and are prone to change over time.

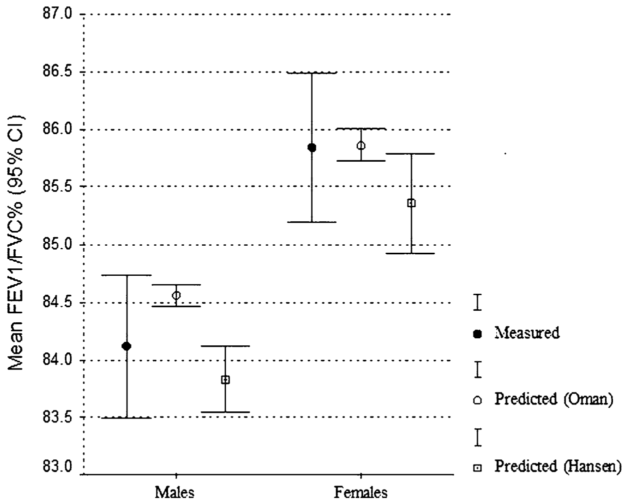

Fig. 1 Comparison of calculated FEV_1/FVC% with its predicted values using our equations and the race- and gender-independent equation suggested by Hansen et al. [17]

Comparing lung function values derived using our prediction equations with the values obtained by using the two selected and widely used equations for Caucasians showed that our predicted FVC was lower by 11–17% in men and 7–14% in women. Similarly, FEV_1 was lower by 7–14% in men and 7–13% in women. The differences in predicted PEFR and FEV_1/FVC% and $FEF_{25–75\%}$ were not as large (2–10%). In contrast, our predicted values were higher than the corresponding values derived using the Pakistani equations with smaller differences in women. Although this may be explained by the ethnic differences, the pattern of difference suggest that the lower predicted reference values of Pakistani men might be due to greater exposure to outdoor pollution compared with Pakistani women. The Pakistani study was conducted in Karachi, the largest city of Pakistan with a population of approximately 13 million, which has heavy traffic and multiple ethnicities [16].

As expected from previous reports [9, 12, 13], the predicted values of our subjects by Jordanian equations were closer to those of Caucasians. Hence, our predicted values for FVC and FEV_1 were lower by approximately 20% in men and 15–18% in women. The use of such equations resulted in classifying >50% of our normal men and 24–39% of our normal women as subnormal. The reasons for the relatively high reference values for Jordanians compared with other populations in the region and other non-Caucasian ethnic groups are not clear [7, 16, 24–26]. Unlike the Jordanian reference values, our predicted values for the various lung function parameters are in close agreement with those from other Arab populations [10–14]. In the only two published reports on normal spirometric values from Saudi Arabia, FVC and FEV_1 were found to be lower and FEV_1/FVC and $FEF_{25–75\%}$ were similar or higher than the corresponding western values [10, 12]. The mean predicted values of FVC and FEV_1 in 276 Libyan men [13], 209 Egyptian men industrial workers [11], and 213 Egyptian women industrial workers [14] also were reported to be lower than their corresponding values derived from western prediction equations.

There are a few limitations in this study. First, there is a sampling bias because the centers were located in a single region. However, this region hosts the capital of Oman and thus attracts citizens from all over the country. Therefore, it is reasonable to consider Muscat, which accommodates one-third of the population of the country, as representative of the urban population of Oman. In addition, as described in the "Methods" section, the enrollment centers were carefully chosen to achieve a reasonably representative sample in a practical and cost-effective manner. Second, comparisons of different prediction equations should have been done in separate groups of healthy subjects. But like most other studies, due to cost and labor and the need to include all the obtained normal values in the derivation of the equations, we used the same study subjects for such comparison. Finally, due to the age range of our study population, the results may not applicable to subjects older than 65 years.

Conclusions

The results of this study provide the lung function predicted equations derived from a relatively large, healthy, nonsmoking, Omani, adult population. The differences in lung function values derived from prediction equations of this study and those derived from Caucasian populations confirms that continued use of such equations for calculating predicted values of lung function for our and perhaps other Arab populations may not be appropriate. Moreover, this study highlights the urgent need to develop reference values for other lung function indices, such as static lung volumes and the pulmonary diffusing capacity, which are lacking in the entire Arab region. Furthermore, studies of lung function in our region and other developing countries should be encouraged because they may contribute to the understanding of the relative roles of genetic and environmental factors that affect lung function development and decline.

Acknowledgments The authors thank Sultan Qaboos University Hospital Management and Professor M. O. Hassan, Head Department of Clinical Physiology, for the support and permission to use the Clinical Physiology Laboratory facilities to conduct the study and Oman Exhibition Center Management for granting our research team a dedicated booth for spirometric measurements free of charge. The authors also thank Mrs. R. Jothi, from the Department of Clinical Physiology for her assistance in spirometric measurements and data entry, and all the volunteers who participated in the study.

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