Karunanayake et al. Int J Respir Pulm Med 2015, 2:2
ISSN: 2378-3516

International Journal of
Respiratory and Pulmonary Medicine

Original Research Article: Open Access

Reference Values of Pulmonary Function Tests for Rural Canadians

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Abstract

Background: Pulmonary function tests are used routinely to evaluate patients with respiratory diseases and those who are at risk of developing respiratory diseases. Lung function prediction equations are generally developed for urban populations and whether these differ on rural population is not well studied. There is limited information on prediction equations for rural populations.

Objective: The purpose of the present study was to derive prediction equations for commonly used pulmonary function tests in a rural Canadian Caucasian population and to examine whether results of tests were comparable with published equations currently in use.

Methods: The Saskatchewan Rural Health Study was a prospective cohort study conducted in 2010-11. Clinical assessments were conducted on 1675 adults and of those, 1609 had satisfactory pulmonary function tests. Ninety two healthy, asymptomatic lifetime nonsmoking rural Caucasian adults were selected to derive rural Canadian predicted equations. The predictive models were compared with three published models (Crapo, Canadian, and Global Lung Function Initiative 2012) for selected tests. In addition to age and height, other factors such as weight and abdominal girth were considered.

Results: Comparisons with published references showed good agreement with Canadian equations and present study for males but less agreement for females. Weight or abdominal girth did not improve the predictive model significantly.

Conclusion: Although there were slight differences, the prediction equations for rural Caucasians were very much similar to the three published equations, of these two were primarily based on urban subjects (Crapo and Canadian). Therefore, all three published studies can be recommended for the prediction of reference values for rural Canadian Caucasians.

Keywords

Rural, Pulmonary function tests, Reference values, Spirometry

Abbreviations

PFTs: Pulmonary Function Tests, ATS: American Thoracic Society, SRHS: Saskatchewan Rural Health Study, SPT: Skin Prick Testing, FEV_1: Forced Expired Volume in one Second, FVC: Forced Vital Capacity, FEF_{25-75}: Maximum Mid-Expiratory Flow Rate, SEE: Standard Error of the Estimate, GLI: Global Lung Function Initiative

Introduction

Pulmonary function tests (PFTs) are used routinely to evaluate patients with respiratory diseases and those who are at risk of developing respiratory diseases [1,2]. Normal lung function values and ranges are calculated according to variables such as age, height and weight, and should be based on measurement techniques in accordance with guidelines published by the American Thoracic Society (ATS) [3,4]. The common practice in recent studies [5,6] for determining normal lung function values has been to define the reference population as being that portion of the total population compared exclusively of healthy, lifetime nonsmokers. Some studies discuss other standards for population differences such as race or ethnicity [1,5,7-9], region or country [2,6,10,11], and urban/rural settings [1,12]. In addition, there may be differences in lung function between populations due to varying occupational and environmental exposures and need to be considered when estimating prediction equations [13,14]. Due to these reasons healthy lifelong nonsmokers in a rural environment may be have different lung function results compared to urban counterparts.

Lung function prediction equations are generally developed for urban populations and whether these differ on rural population is not well studied. There is limited information on prediction equations for rural populations. A recent study conducted in Saskatchewan consists of rural Canadian Caucasian population who are mainly exposed to farming and other rural exposures. In our previous studies [15,16], we have used Crapo equations (based on urban Caucasian population) to predict lung function values of rural populations. In this report we

Citation: Karunanayake CP, Dosman JA, Hagel L, Rennie DC, Lawson JA, et al. (2015) Reference Values of Pulmonary Function Tests for Rural Canadians. Int J Respir Pulm Med 2:021

Received: June 06, 2015: **Accepted:** June 19, 2015: **Published:** June 22, 2015

would like to investigate whether or not it is appropriate to use prediction equations (such as Crapo) to predict lung function of rural populations by comparing the predicted lung function values based on our study population with those obtained from other established prediction equations [1,5,6].

Methods

Study design for adult baseline survey

The Saskatchewan Rural Health Study (SRHS) was a prospective rural cohort and at present, the baseline survey information has been collected. The rural population was defined as consisting of those persons living in towns and municipalities outside the commuting zone of larger urban centres with a population of 10,000 or more [17]. In 2006, there were 44,329 farm enterprises in Saskatchewan encompassing 111,600 household residents [18]. The baseline survey for adults consisted of three stages: (1) recruitment of populations from rural municipalities and small towns; (2) administration of a mail out household questionnaire; (3) clinical assessment that involved anthropometric measures, lung function measurements, and allergy testing on sub-population. Details of the study design are provided elsewhere [19]. In brief, Dillman's method, which involves a series of mail contacts with all prospective participants, was utilized to recruit study participants [19,20]. After excluding ineligible households information on variables of demographics, lifestyle factors, occupational exposures, and socio-economic status based on the Population Health Framework [21,22] was collected by self-administered questionnaires. The study population comprised 8261 individuals (males and females, 18 years of age or older) from 4624 households living in 32 rural municipalities and 15 rural towns in the study area. The study was approved by the Biomedical Research Ethics Board of the University of Saskatchewan, Canada. The SRHS was conducted with the understanding and informed consents of the all participants.

Clinical assessments

The final question on the baseline questionnaire was 'Would you be willing to be contacted about having breathing and/or allergy tests at a nearby location?' Those who responded positively to this question were sent a letter of invitation to participate in a clinical assessment. Research nurses trained in spirometry and allergy assessment and located in each study quadrant telephoned each household of consenting participants to arrange a time and a place (usually no greater than 60 kilometers from their residence) for this clinical assessment. Mobile clinics were set up in small towns located in the study area. The clinical testing consisted of lung function testing with spirometry, allergy skin prick testing (SPT), blood pressure, and anthropometric measurements (height, weight, abdominal girth). The protocol is described below.

Measurements and selection criteria

Blood pressure was measured as recommended by the Canadian Coalition for High Blood Pressure [23]. Spirometry was completed using the forced expiratory maneuver. The measures of forced expired volume in one second (FEV_1), forced vital capacity (FVC), FEV_1/FVC ratio, and maximum mid-expiratory flow rate (FEF_{25-75}) were obtained via Sensormedics (Anaheim, CA) dry rolling seal volume displacement spirometers [16,24,25]. Measurements were taken according to standards of the American Thoracic Society [3,4]. There were 3209 persons who consented on the questionnaire to having further testing. Of those, 2863 individuals aged 18-75 years were contacted of which 1675 persons completed clinical testing and 1609 had satisfactory pulmonary function tests. A technically unsatisfactory pulmonary function test is defined as if excessive

Table 1: Physical Characteristics of normal subjects in SRHS

	Men n=46		Women n=46	
	Range	Mean ± SD	Range	Mean ± SD
Age in years	20.0-69.0	50.9 ± 11.9	27.0 - 68.0	49.6 ± 11.2
Height, cm	144.5-190.0	175.9 ± 8.4	151.0-177.0	163.4 ± 5.1
Weight, Kg	42.1-132.0	86.4 ± 14.8	50.9- 88.5	68.1 ± 8.6
Abdominal Girth, cm	76.0-134.0	97.8 ± 11.4	64.0-102.0	84.1 ± 8.1
Age in years	**Men n=46 n (%)**		**Women n=46 n (%)**	
20-29	5 (10.9)		3 (6.5)	
30-39	4 (8.7)		6 (13.0)	
40-49	5 (10.9)		12 (26.1)	
50-59	19 (41.3)		15 (32.6)	
60-69	13 (28.3)		10 (21.7)	

Table 2: Pulmonary function test prediction equations for rural males

Test, Units	Equations	R^2	SEE
FVC, L	$-6.068^{**} + 0.073H^{\dagger} - 0.034A^{\dagger}$ (SRHS)	0.678	0.540
	$-6.616^{**} + 0.079H^{\dagger} - 0.033A^{\dagger} - 0.007W$ (SRHS)	0.687	0.539
	$-5.958^{**} + 0.077H^{\dagger} - 0.030A^{\dagger} - 0.011AB$ (SRHS)	0.692	0.534
	$-5.473 + 0.067H - 0.025A$ [6]	0.560	0.589
	$-4.650 + 0.060H - 0.0214A$ [1]	0.540	0.644
FEV_1, L	$-3.655^{**} + 0.052H^{\dagger} - 0.031A^{\dagger}$ (SRHS)	0.729	0.376
	$-3.933^{**} + 0.055H^{\dagger} - 0.031A^{\dagger} - 0.003W$ (SRHS)	0.733	0.378
	$-3.589^{**} + 0.055H^{\dagger} - 0.029A^{\dagger} - 0.007AB$ (SRHS)	0.738	0.374
	$-2.832 + 0.047H - 0.030A$ [6]	0.620	0.500
	$-2.190 + 0.041H - 0.0244A$ [1]	0.640	0.486
FEF_{25-75}, L	$+0.299 + 0.032H^{*} - 0.041A^{\dagger}$ (SRHS)	0.388	0.753
	$+0.531 + 0.029H - 0.042A^{\dagger} + 0.003W$ (SRHS)	0.389	0.761
	$+0.305 + 0.032H^{*} - 0.041A^{\dagger} -0.001AB$ (SRHS)	0.388	0.762
	N/A		
	$+2.133 + 0.0204H - 0.0380A$ [1]	0.420	0.962
FEV_1/FVC	$+111.397^{\dagger} - 0.151H^{*} - 0.110A^{*}$ (SRHS)	0.150	4.189
	$+112.751^{\dagger} - 0.167H - 0.112A^{*} + 0.017W$ (SRHS)	0.153	4.233
	$+111.279^{\dagger} - 0.156H - 0.114A + 0.012AB$ (SRHS)	0.151	4.238
	$+109.396 - 0.113H - 0.210A$ [6]	0.240	5.821
	$+110.49 - 0.130H - 0.152A$ [1]	0.260	4.780

Abbreviations: FVC: Forced Vital Capacity, FEV_1: Forced Expiratory Volume in the first second, FEF_{25-75}: Forced Expiratory Flow during the middle half of the Forced Vital Capacity, H: Height in cm, A: Age in years, W: Weight in Kg, AB: Abdominal girth in cm, R^2: Coefficient of determination, SEE: Standard error of the estimate, SRHS: Saskatchewan Rural Health Study, Statistically significant regression coefficients were indicated using * if p-value<0.05; ** if p-value<0.01; † if p-value<0.001.

Table 3: Pulmonary function test prediction equations for rural females

Test, Units	Equations	R^2	SEE
FVC, L	$-1.562 + 0.044H^{\dagger} - 0.042A^{\dagger}$ (SRHS)	0.710	0.374
	$-1.336 + 0.048H^{\dagger} - 0.040A^{\dagger} - 0.014W^{*}$ (SRHS)	0.742	0.357
	$0.944 + 0.039H^{\dagger} - 0.039A^{\dagger} - 0.022AB^{**}$ (SRHS)	0.777	0.333
	$-3.335 + 0.049 H - 0.024A$ [6]	0.660	0.427
	$-3.590 + 0.0491H - 0.0216A$ [1]	0.740	0.393
FEV_1, L	$+0.493 + 0.026H^{**} - 0.037A^{\dagger}$ (SRHS)	0.806	0.234
	$+0.629 + 0.028H^{\dagger} - 0.036A^{\dagger} -0.009W^{*}$ (SRHS)	0.825	0.225
	$+1.833 + 0.023H^{**} - 0.035A^{\dagger} - 0.012AB^{**}$ (SRHS)	0.838	0.216
	$-1.901 + 0.037H - 0.025A$ [6]	0.730	0.340
	$-1.578 + 0.0342H - 0.0255A$ [1]	0.800	0.326
FEF_{25-75}, L	$+6.073^{**} - 0.007H - 0.044A^{\dagger}$ (SRHS)	0.602	0.399
	$+6.094^{**} - 0.006H - 0.044A^{\dagger} + 0.001W$ (SRHS)	0.603	0.403
	$+5.613^{*} - 0.006H - 0.044A^{\dagger} + 0.004AB$ (SRHS)	0.605	0.402
	N/A		
	$+2.683 + 0.0154H - 0.0460A$ [1]	0.600	0.792
FEV_1/FVC	$+128.74^{\dagger} - 0.263H^{*} - 0.126A^{**}$ (SRHS)	0.281	3.123
	$+127.81^{\dagger} - 0.279H^{**} - 0.133A^{**} + 0.059W$ (SRHS)	0.239	3.117
	$+113.22^{\dagger} - 0.233H^{*} - 0.142A^{**} + 0.137AB^{*}$ (SRHS)	0.317	2.954
	$+ 104.509 - 0.089H - 0.182A$ [6]	0.200	5.680
	$+126.58 - 0.2020H - 0.252A$ [1]	0.430	5.260

Abbreviations: FVC: Forced vital capacity, FEV_1: Forced Expiratory Volume in the First Second, FEF_{25-75}: Forced Expiratory Flow during the Middle Half of the Forced Vital Capacity, H: Height in cm, A: Age in years, W: Weight in Kg, AB: Abdominal Girth in cm, R^2: Coefficient of determination, SEE: Standard Error of the Estimate, SRHS: Saskatchewan Rural Health Study, Statistically significant regression coefficients were indicated using * if p-value<0.05; ** if p-value<0.01; † if p-value<0.001.

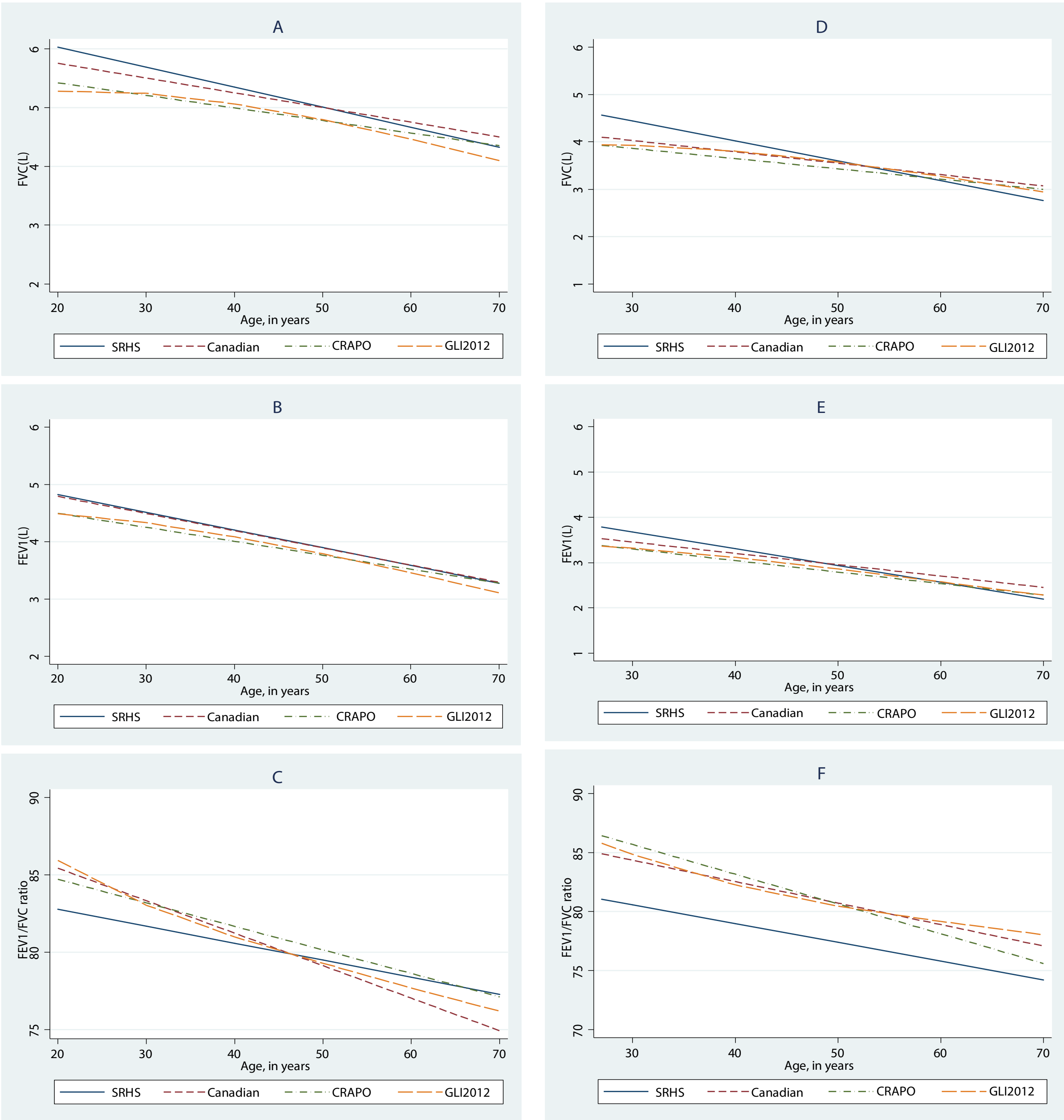

Figure 1: Predicted Forced Vital Capacity (FVC) (A), Predicted Forced Expiratory Volume in 1 s (FEV_1) (B) and FEV_1/FVC ratio (C) by age for 20 to 70 years old men 175cm in height and Predicted Forced Vital Capacity (FVC) (D), Predicted Forced Expiratory Volume in 1 s(FEV_1) (E) and FEV_1/FVC ratio (F) by age for 27 to 70 years old women 165 cm in height using the present study(SRHS), Canadian, Crapo and GLI2012 equations

hesitation of false start, coughing during the first second of maneuver, glottis closure, a leak in the system or around the mouthpiece, and an obstructed mouthpiece [3,4]. For this analysis, 92 rural Caucasian normal healthy subjects were selected (46 males and 46 females). These were subjects those who met the following criteria defined as "normal": a lifetime non-smoker; free of any of following non-respiratory chronic conditions: diabetes, heart disease, heart attack, hardening of the arteries, high blood pressure; free of any of following respiratory/chest illnesses: attack of bronchitis, pneumonia, hay fever, sinus trouble, chronic bronchitis, emphysema, chronic obstructive pulmonary disease, sleep apnea, asthma, cystic fibrosis, tuberculosis and other chest illnesses; and no respiratory symptoms (cough, phlegm or wheeze) or shortness of breath.

Data analysis

Regression models for each PFT, with age, height, weight and abdominal girth as predictive covariates were obtained for each sex. The goodness of fit of the models was determined by their coefficient of determination (R^2) and standard error of the estimate (SEE or residual SD) and analysis of residuals. The transformation of the dependent variable into logarithms was tested and did not improve the predictive ability of the model substantially. Assumption of normality of the dependent variables was tested using the Shapiro-Wilk test. If the p-value of the Shapiro-Wilk test was greater than 0.05, the data was considered normal [26]. Predicted values of pulmonary function tests were calculated using Canadian [6], Crapo [1] and Global Lung Function Initiative 2012 (GLI2012) [5] equations and were compared graphically.

Results

The mean, standard deviation (SD) and range of age, height, weight and abdominal girth are given in Table 1. The subjects ranged from 20 to 69 years. Values of R^2 and SEE from the predicted equations for the present study (SRHS) and from two previous studies (Canadian study [6] and Crapo [1]) are shown in Table 2 (for males)

ISSN: 2378-3516

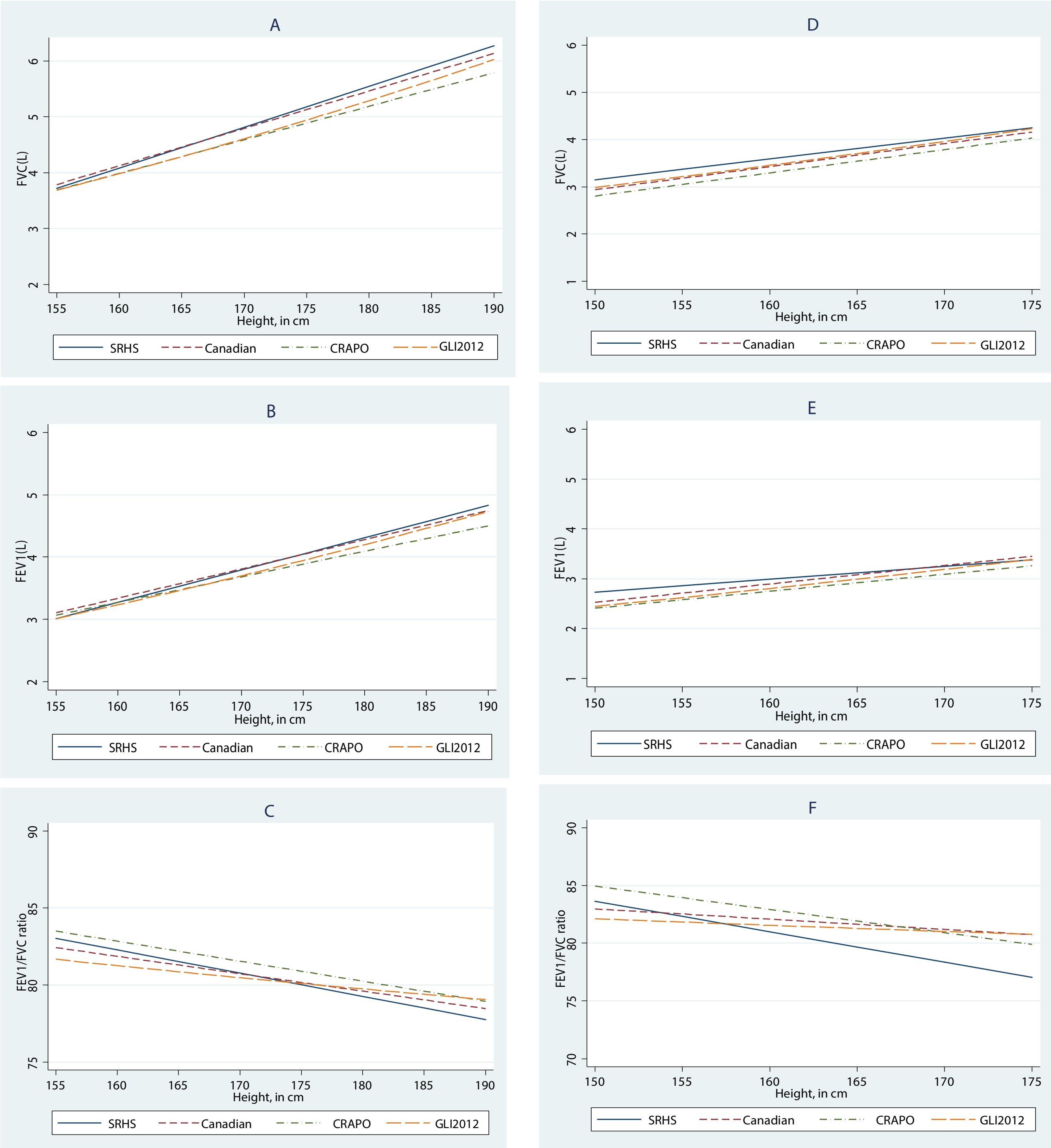

Figure 2: Predicted Forced Vital Capacity (FVC) (A), Predicted Forced Expiratory Volume in 1 s(FEV_1) (B) and FEV_1/FVC ratio (C) by height for 155cm to 190cm men 45 years old age and Predicted Forced Vital Capacity (FVC) (D), Predicted Forced Expiratory Volume in 1 s(FEV_1) (E) and FEV_1/FVC ratio (F) by height for 150cm to 175cm women 45 years old age using the present study(SRHS), Canadian, Crapo and GLI2012 equations.

and Table 3 (for females). For the SRHS, both weight and abdominal girth were not significant predictors for all four PFTs for males. For females, both weight and abdominal girth were significant predictors for FVC and FEV_1, and abdominal girth was significant predictor for FEV_1/FVC ratio. But, there was no significant difference in model fit when abdominal girth was added to the model for females instead of weight. Overall, there was no significant difference in model fit adding covariates weight or abdominal girth to the model for females with predictive covariates age and height. Therefore, the models with predictive covariates age and height were used for comparison purposes. For the SRHS regression models with age and height as predictive covariates, R^2 was greater for FVC and FEV_1 and R^2 was lower for FEF_{25-75} and FEV_1/FVC ratio for males compared to the Canadian [6] and Crapo [1] predicted equations. For females, R^2 values for the SRHS prediction equations were greater for FVC, FEV_1 and FEV_1/FVC ratio compared to Canadian study prediction equations. For the SRHS prediction equations, SEE was lower than the value for all PFTs compared to predicted equations of other two studies for both males and females. We were unable to compare GLI2012 equations as different methodology was used for the computation of prediction equations. Hence, there were no available published values of R^2 and SEE from GLI2012 equations for Caucasians.

Figures 1-3 depict the graphical comparison of predicted pulmonary function values based on the four different prediction equations, namely, SRHS, Canadian [6], Crapo [1], and GLI2012 [5]. As indicated in Figure 1 (Panel B), predicted values of FEV_1, when corrected for height and age appear to be similar for ages 20 to 70 years old men 175cm in height based on the SRHS and the Canadian study prediction equations [6]. The predicted values of FVC for males based on Crapo [1] and GLI2012 [5] equations are lower than

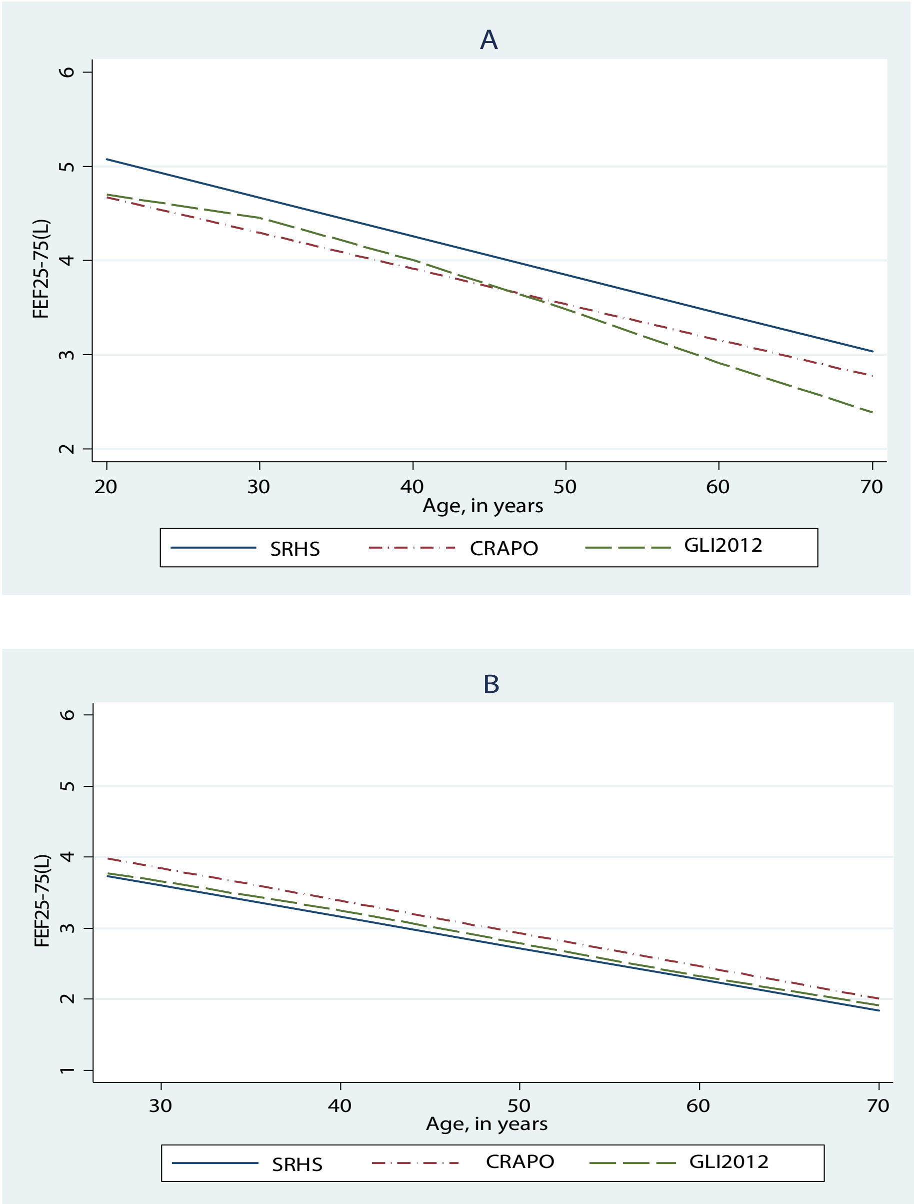

Figure 3: Predicted Forced Expiratory Flow during the middle half of the Forced Vital Capacity (FEF_{25-75}) for a male 175cm in height for 20 to 70 years (A), Predicted forced expiratory flow during the middle half of the forced vital capacity (FEF_{25-75}) for a female 165cm in height for 27 to 70 years (B) using the present study (SRHS), Crapo and GLI2012 equations.

those based on equations of the Canadian [6] and the SRHS (Figure 1,Panel A). For ages 20-45 years old, 175cm in height men, values for FEV_1/FVC ratio based on SRHS equations are lower than those of the three other studies (Figure 1,Panel C). Values of FVC and FEV_1 were similar for the Canadian [6] and the SRHS prediction equations for heights 155 to 190 cm men 45 years of old age when corrected for height and age (Figure 2,Panel A & B). The FEV_1/FVC ratio are higher using Crapo equations [1] than predicted values obtained using the Canadian, GLI2012 and the SRHS prediction equations for heights 155 to 185 cm and 45 years of old men (Figure 2,Panel C).

For FVC, we observed slightly higher values using the SRHS prediction equations compared to the predictions from other three studies for ages 27 to 55 and 165cm tall female (Figure 1,Panel D) and for heights 150 to 175cm and 45 years old female (Figure 2,Panel D). For FEV_1, we observed slightly higher values using the SRHS prediction equations compared to the values predicted from other three studies for ages 27 to 45 years and 165cm tall female and for heights 150 to 165cm and 45 years old female (Figure 1,Panel E and Figure 2,Panel E respectively). Also we observed slightly lower values for FEV_1 using prediction equations of the SRHS compared to Canadian study [6] for ages 50 to 70 years and 165cm tall female (Figure 1,Panel E). The SRHS predicted values for FEV_1/FVC ratio were lower than those predicted using prediction equations of the Canadian [6], GLI2012 [5] and Crapo [1] for females with ages 27 to 70 (Figure 1,Panel F) and heights 157 to 175cm (Figure 2,Panel F).

For the Canadian study [6], the prediction equations for FEF_{25-75} was not available, hence the comparison of predicted FEF_{25-75} values with the SRHS predicted equations was not possible.

However, the predicted FEF_{25-75} values using SRHS equations are higher than those using prediction equations for the GLI2012 [5] and Crapo study [1] for males of 175cm aged from 20 to 70 years (Figure 3,Panel A). The predicted FEF_{25-75} values were not much different using the SRHS and GLI2012 [5] prediction equations for females of 165cm aged from 27 to 70 years. The predicted FEF_{25-75} values using SRHS equations are lower than those using prediction equations of the GLI2014 [5] and Crapo study [1] for females of 165cm aged from 27 to 70 years (Figure 3,Panel B). However there were differences of FEF_{25-75} predicted values using the predicted equations of three studies (Crapo, GLI2012 and SRHS) for 45 year old male or female with heights ranges from 155 to 190cm and 150 to 175cm, respectively.

Discussion

We have modeled equations for several PFTs based on data available for normal healthy, rural Caucasian lifetime nonsmokers from Saskatchewan, Canada. We found that, although there were slight differences, the predictions of FVC and FEV_1 were very much similar to those based on the Canadian study [6] equations for males, which mostly included urban subjects. Therefore there is no difference in PFTs for males with respect to urban or rural setting. For females, the predictions of FVC and FEV_1 based on the SRHS equations did not show very good agreement with predicted values obtained using Canadian [6], Crapo [1] and GLI2012 [5] equations. For both males and females we did not see a very good agreement of FEV_1/FVC ratio predictions using the prediction equations of the present study and other three studies [1,5,6]. There was a very good agreement for females of FEF_{25-75} predicted values of the SRHS equations with GLI2012 [5] equations and we did not observe this in males.

We thought that rural Caucasians might have values for pulmonary function that would be affected by the high rates of obesity in rural people [27]. However that did not seem to be true. We did not observe significant improvement of the fit of the predictive models when covariates weight and abdominal girth were included in the models. Supporting this idea, a recent study reported that there was no effect from obesity on spirometry tests [28].

Caucasians were selected in all four studies to derive prediction equations and were believed to have a similar ethnic origin. Crapo's model was generated in the United States in Caucasian urban populations and the Canadian study, mostly included urban subjects from Canada. The GLI study included Caucasians from Brazil, Australia, Canada, USA, Israel, Mexican Americans, Chile, Mexico, Uruguay, Venezuela, Algeria, Tunisia and many European countries. All four studies complied with ATS recommendations and techniques. Differences in prediction equations based on these studies could be due to several reasons, such as, sample size variations among the four studies and rural versus urban populations. It can be assumed that the rural populations tend to be more homogeneous than urban populations in terms of environmental exposures. However, these findings on differences in prediction equations warrant further investigation.

A strength of this study was that the selected subjects lived in a rural setting and no urban residents were included in the SRHS. This helped us to establish prediction equations for rural Canadian Caucasians. One of the limitations of the present study is the relatively small sample size with 46 males and 46 females. According to Schneider et al. [29] for linear regression model in general, the number of observations must be at least 20 times greater than the number of variables under study. As our sample sizes are greater than 40 for males and females, the multiple linear regression models with age and height are reasonable for prediction of PFTs. However, due to small samples results from models with three variables ([age, height, weight] and [age, height, abdominal girth]) need to be interpreted with caution. Another potential limitation was that the selection criteria depended on participants consent to taking part in clinical assessment and then screening of self-reported responses of the subjects, which can lead to biased results [30]. In the present study subjects were screened as normal healthy subjects if they were asymptomatic to respiratory diseases and symptoms and lifetime nonsmokers using the responses from self-reported questionnaire. In the other three studies participants were highly screened with a clinical examination and laboratory tests [1,5-6]. Another limitation was the length of rural residency was unknown. Currently, the participants lived in rural area, but do not know how long they were there.

Conclusions

In summary, we compared our models for selected PFTs with Canadian, Crapo and GLI2012 prediction equations, and found them to be fairly similar overall, although there were some differences for both males and females. Therefore, the prediction equations from all three published studies [1,5,6] can be recommended for the prediction of reference values for rural Canadian Caucasians.

Acknowledgements

The Saskatchewan Rural Health Study Team consists of: James Dosman, MD (Designated Principal Investigator, University of Saskatchewan, Saskatoon, SK Canada); Dr. Punam Pahwa, PhD (Co-principal Investigator, University of Saskatchewan, Saskatoon SK Canada); Dr. John Gordon, PhD (Co-principal Investigator, University of Saskatchewan, Saskatoon SK Canada); Yue Chen, PhD (University of Ottawa, Ottawa Canada); Roland Dyck, MD (University of Saskatchewan, Saskatoon SK Canada); Louise Hagel (Project Manager, University of Saskatchewan Saskatoon SK Canada); Bonnie Janzen, PhD (University of Saskatchewan, Saskatoon SK Canada); Chandima Karunanayake, PhD (University of Saskatchewan, Saskatoon SK Canada); Shelley Kirychuk, PhD (University of Saskatchewan, Saskatoon SK Canada); Niels Koehncke, MD (University of Saskatchewan, Saskatoon SK Canada); Joshua Lawson, PhD, (University of Saskatchewan, Saskatoon SK Canada); William Pickett, PhD (Queen's University, Kingston ON Canada); Roger Pitbaldo, PhD (Professor Emeritus, Laurentian University, Sudbury ON Canada); Donna Rennie, RN, PhD, (University of Saskatchewan, Saskatoon SK Canada); Ambikaipakan Senthilselvan, PhD (University of Alberta, Edmonton, AB, Canada). This study was funded by a grant from the Canadian Institutes of Health Research "Saskatchewan Rural Health Study", Canadian Institutes of Health Research MOP-187209-POP-CCAA-11829. We are grateful for the contributions of the rural municipality administrators and the community leaders of the towns included in the study that facilitated access to the study populations and to all of participants who donated their time to complete and return the survey.

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ISSN: 2378-3516