Values of Impulse Oscillometry in Healthy Mexican Children and Adolescents

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BACKGROUND: The impulse oscillometry system (IOS) is increasingly used to evaluate lung function, but individual results must be compared with appropriate reference values. We aimed to obtain such reference values in Mexican children and adolescents. METHODS: Healthy subjects were recruited from kindergartens and schools after their parents signed a consent letter. Respiratory system impedances (Zrs), resistances (Rrs), and reactances (Xrs) were measured at 5, 10, 15, and 20 Hz, and the resonant frequency, reactance area, and difference between Rrs5 minus Rrs20 were also calculated. RESULTS: After exclusion of 4 children who were unable to perform an acceptable IOS recording, the final population comprised 283 children (153 females) 2.7–15.4 y of age. As a group, girls tended to have lower Xrs5 and higher Zrs20 and Rrs20 values. In bivariate analyses, all IOS variables had good correlation with age, height, and weight, and a better straight-line fitting was obtained through data transformation to the $\log_{10}$ (age) or reciprocal (height and weight) values. Comparison of regression lines revealed small differences between males and females, especially in Xrs. Multiple linear regression analysis identified height as the most influential variable in the majority of IOS variables, but age also accounted for a moderate-to-large influence in the regression models in many IOS variables. CONCLUSIONS: In this study, we generated reference equations for each IOS variable in healthy children and adolescents. Although these equations were generated in a Mexican population, they are probably also applicable in other Latin American populations with the same ethnic background. *Key words: impulse oscillometry; reference values; normal values; respiratory impedance; respiratory reactance; respiratory resistance.* [Respir Care 2015;60(1):119–127. © 2015 Daedalus Enterprises]

Introduction

Pulmonary function tests are useful tools for diagnosis, evaluation, and follow-up of patients with respiratory diseases. Although spirometry is the most common of these tests, it demands the full cooperation of the subject, which is not always possible to obtain, especially in young chil-

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dren. The impulse oscillometry system (IOS) has been increasingly used due to its technical simplicity, because measurements are taken while the subject breathes at tidal volume. Briefly, the basis of this technique is as follows.[1] The equipment uses a loudspeaker to send to the respiratory system a set of sound pulses or clicks at a rate of ~5 pulses/s. Each click is integrated by sinusoidal sound waves of varying frequencies (from 5 to 20 Hz), overlapped in a square wave. Every click produces a pressure pulse (~2 cm H_2O) that causes small pressure and flow changes, which are superimposed onto the respective normal pressure and flow curves generated during tidal breathing. Using fast Fourier transform analysis, the equipment separates modifications occurring at specific frequencies (5, 10, 15, and 20 Hz). In this analysis, the ratio of the pressure to flow changes yields the magnitude of the respiratory system impedance (Zrs), and because Zrs is a vector, its direction is determined by the lag phase between pressure and flow changes. Finally, decomposition of this vector in the real and imaginary axes yields the values for respiratory system resistance (Rrs) and reactance (Xrs), respectively. A valuable advantage of IOS, not shared by other techniques, is the possibility of partitioning the lung region being evaluated. Thus, whereas responses to 5 Hz are considered to represent impedance from total airways, those obtained at 20 Hz are preferentially generated in central airways. In addition, it is considered that Rrs mostly reflect resistive components (mainly due to resistance to air flow), whereas Xrs reflect inertive and capacitive components (mainly generated in lung and chest wall tissues).[2]

Several studies have shown that IOS correlates well with spirometric indexes, and that it is comparable to, or even more sensitive than, spirometry for detecting airway responses during bronchodilation or bronchoconstriction.[3-5] Moreover, in patients with asthma, IOS is useful to assess therapeutic responses to corticosteroids[6] and to predict ongoing loss of disease control.[7] Thus, IOS appears to be a valuable tool for managing lung diseases. However, as with any other test, the result of an individual IOS test needs to be compared with an appropriate set of reference values generated in healthy population of the same age, gender, and ethnicity.[8] To our knowledge, there are no published reports of IOS reference values for Mexican or Latin American children; thus, the aim of our study was to obtain such reference equations, evaluating potential differences between males and females.

QUICK LOOK

Current knowledge

Impulse oscillometry is used to measure respiratory system resistance and reactance during normal tidal breathing. The advantages of this technique are simplicity and the ability to partition lung regions (central vs peripheral airways). Normal ranges across populations for impulse oscillometry are not yet defined.

What this paper contributes to our knowledge

In a study of 283 Mexican children and adolescents, reference equations for impulse oscillometry variables were generated using age, gender, and height and weight. Height was the most important variable followed by age. These equations may have generalizability across other ethnic groups of similarly aged subjects.

Methods

The study protocol was approved by the science and bioethics committee of the Instituto Nacional de Enfermedades Respiratorias (approval C20-11). The study population was recruited from among alumni attending kindergartens and primary or secondary schools located in the metropolitan area of Mexico City. After the corresponding educational authorities gave their permission for the study, a brief health questionnaire and a consent letter were sent to the parents. Children and adolescents whose parents agreed with their participation were included in the study if they fulfilled the following criteria: (1) without chronic illnesses including heart, liver, kidney, and respiratory diseases (asthma, wheezing, rhinosinusitis); (2) without past history of prematurity, pneumonia, bronchiolitis, or regular exposure to environmental tobacco or biomass smoke; (3) absence of any acute respiratory morbidity in the past 15 days; (4) without suspicion of sleep apnea/hypopnea syndrome or gastroesophageal reflux.

Impulse Oscillometry Procedure

IOS was carried out with commercial equipment (MS-IOS, Erich Jaeger, CareFusion, San Diego, California). According to the manufacturer's instructions, volume and pressure calibration of the equipment was verified on a daily basis with a certified 3-L syringe (maximal variability 3%) and with a pressure calibrator (0.2 kPa impedance) with maximal pressure variability of $\pm$ 0.01 kPa. Additionally, linearity at 3 different flows ($<$ 2, 4–6, and $>$ 8 L/s) was corroborated on a weekly basis. On the day of the study, subjects were submitted to a physical examination, and their weight and standing height were measured (scales models 206 and 769, Seca, Hamburg, Germany). The IOS procedure was performed according to major recommendations published by several authors.[9-11] Briefly, with the subject in the sitting position and wearing a nose clip, the procedure was explained in plain language and the child or adolescent was allowed to become accus-

Table 1. Anthropometric Features in Healthy Children and Adolescents Submitted to Impulse Oscillometry System Measurement

Variable	All (*N* = 283)		Females (*n* = 153)		Males (*n* = 130)		*P**
	Median	Q1, Q3	Median	Range	Median	Range	
Anthropometric features							
Age (y)	8.3	5.1, 10.5	8.0	2.7–15.2	8.4	3.0–15.4	.38
Weight (kg)	25.5	18.9, 34.6	24.8	12.0–69.4	26.2	13.6–76.6	.38
Height (cm)	125.0	109.0, 137.3	123.3	85.5–163.5	125.1	93.0–170.8	.31
BMI (kg/m^2)	16.7	15.6, 18.6	16.7	13.1–27.8	16.7	10.2–27.8	.85

* Comparison between males and females (Mann-Whitney U-test).
Q1 = quartile 1
Q3 = quartile 3
BMI = body mass index

tomed to the equipment. The subject was asked to breath into the equipment's mouthpiece, which was coupled with an antibacterial filter. While under quiet tidal breathing and with cheeks supported by a research collaborator, 3 IOS measurements were carried out, each lasting 30 s and performed 1 min apart. Acceptability criteria of the recording included lack of visually detected artifacts and a coherence (ie, correlation between input and output signals) of at least 0.6 at 5 Hz and 0.9 at 10 Hz.

Variability of IOS results obtained in the same subject was assessed by 3 different approaches: (1) the intrameasurement coefficient of variation (im-CV), that is, the variability of the three 30-s IOS measurements used to average the final IOS result; (2) the within-occasion or short-term variability, that is, the comparison of 2 IOS results obtained 30 min apart; and (3) the between-occasion or long-term variability, that is, the comparison of 2 IOS results obtained 15 d apart. For the last 2 approaches, a group of 30 children under 6 y of age were randomly selected, and 2 additional IOS measurements were performed 30 min and 15 d later.

Data Analysis

IOS variables included in the analyses were Zrs, Rrs, and Xrs, all measured at 5, 10, 15, and 20 Hz, as well as the resonant frequency (Fres), reactance area (AX), and difference between Rrs5 minus Rrs20 (DRrs5 − Rrs20). Degree of variability was evaluated for each IOS variable by using the coefficient of variation (CV = 100 × standard deviation/mean, expressed in percentage), and the coefficient of repeatability ($CR = 1.96 \times \sqrt{\sum[x_1 - x_2]^2/[n - 1]}$, expressed in the same units as the respective variable).

The majority of IOS variables did not follow normal distribution because they were skewed to the right (Zrs, Rrs, and AX) or left (Xrs). Thus, the nonparametric Mann-Whitney U-test was used to compare males and females; the Spearman rank correlation coefficient (r_S) was used to evaluate associations between every IOS variable and age, height, or weight; and the Friedman test followed by the Wilcoxon signed-rank test with Bonferroni correction was used to evaluate changes of IOS values at 30 min and 15 d. In the majority of bivariate regressions, data were transformed into the $\log_{10}$ (age) or reciprocal (height, weight) values to achieve better linearity. IOS values with standardized residuals larger than z = 3.3 were considered as potential outliers, and, after careful examination of individual cases, some of these values were eliminated from

Table 2. Values of Impulse Oscillometry System Parameters Measured in 283 Healthy Children and Adolescents

Variable	Median	Q1, Q3
Zrs5	0.72	0.54, 0.98
Zrs10	0.58	0.44, 0.80
Zrs15	0.51	0.40, 0.73
Zrs20	0.47	0.36, 0.65
Rrs5	0.67	0.50, 0.89
Rrs10	0.55	0.43, 0.77
Rrs15	0.50	0.39, 0.71
Rrs20	0.47	0.36, 0.64
DRrs5-Rrs20	0.19	0.12, 0.27
Xrs5	−0.23	−0.33, −0.17
Xrs10	−0.10	−0.20, −0.10
Xrs15	−0.10	−0.13, 0.03
Xrs20	0.00	−0.10, 0.01
Fres	21.67	19.00, 24.67
AX	1.70	0.93, 2.81

* Comparison between males and females (Mann-Whitney U-test).
Q1 = quartile 1
Q3 = quartile 3
Zrs = respiratory system impedance, followed by the frequency at which measured (5, 10, 15, or 20 Hz), all expressed in kPa/L/s
Rrs = respiratory system resistance, followed by the frequency at which measured (5, 10, 15, or 20 Hz), all expressed in kPa/L/s
DRrs5 − Rrs20 = difference of Rrs5 minus Rrs20, in kPa/L/s
Xrs = respiratory system reactance, followed by the frequency at which measured (5, 10, 15, or 20 Hz), all expressed in kPa/L/s
Fres = resonant frequency, in Hz
AX = area of reactance, in kPa/L

the analysis. Finally, multivariate linear regression was used to generate the reference equations for each IOS variable. Statistical significance was set at 2-tailed $P < .05$.

Results

From 789 children whose parents accepted the participation of their child in the study, 502 did not fulfill one or more selection criteria, mainly because they had experienced an upper airway infection in the last 15 days or had been catalogued as having airway hyperresponsiveness or gastroesophageal reflux or had regular exposure to indoor wood smoke or tobacco smoke. In addition, 4 children were eliminated from the study because they did not perform acceptable IOS recordings. Thus, the final population comprised 283 children, aged 2.7–15.4 y, including 153 females and 130 males.

The anthropometric features of the study population can be observed in Table 1, and no differences could be detected between males and females. Table 2 contains the grouped values for each IOS variable. Comparison between genders showed that the only 3 variables close to reaching statistical significance were Xrs5, which was slightly lower in females (median [range], −0.23 [−0.73 to −0.07] vs males −0.20 [−0.67 to −0.10], $P = .056$), as well as Zrs20 and Rrs20, which were slightly higher in females (0.48 [0.38 to 0.68] vs males 0.45 [0.36 to 0.61], $P = .083$, and 0.48 [0.21 to 1.10] vs males 0.45 [0.21 to 0.95], $P = .085$, respectively, data not illustrated).

As can be seen in Table 3, in the baseline measurement, Zrs, Rrs, and Fres exhibited relatively small intrameasurement variability (im-CV <10%), whereas for DRrs5 − Rrs20, Xrs, and AX, the im-CV ranged from 20.8% to 62.6%. The im-CV values did not differ between males and females (data not shown), and this pattern was essentially the same at 30 min and at 15 d. Interestingly, evaluation of the percentage change of the additional measurements made in a subpopulation of 30 children under the age of 6 y showed that respiratory impedances and resistances tended to be lower at 30 min. Furthermore, this lower tendency reached statistical significance in Zrs20 and Rrs20 at day 15, and the lower values of Rrs20 probably explain concurrent widening of DRrs5 − Rrs20 at day 15.

In bivariate analyses, all IOS variables had good correlation coefficients with age, height, and weight, ranging

Table 3. Variability of IOS Measurements in Healthy Children and Adolescents

IOS Variable	Baseline im-CV* (n = 283)	Variability at 30 min (n = 30)			Variability at 15 d (n = 30)		
		im-CV*	CR	% Change†	im-CV*	CR	% Change†
Zrs5	7.9	9.5	0.27	−0.8 (−14.1, 12.7)	9.2	0.42	−1.1 (−18.4, 42.0)
Zrs10	8.2	8.1	0.26	−2.7 (−15.0, 13.3)	11.2	0.38	−4.0 (−28.3, 22.3)
Zrs15	8.9	9.5	0.28	−3.3 (−13.9, 18.0)	8.8	0.30	−4.9 (−24.2, 15.1)
Zrs20	9.4	8.4	0.19	−1.7 (−14.6, 19.1)	11.9	0.34	−9.5 (−36.4, 19.0)‡
Rrs5	8.9	11.2	0.29	0 (−18.3, 16.7)	10.5	0.42	0.3 (−20.8, 41.2)
Rrs10	8.3	7.5	0.22	−3.1 (−11.3, 12.9)	13.8	0.39	−2.9 (−28.3, 17.6)
Rrs15	9.0	10.1	0.28	−3.0 (−13.2, 28.6)	8.7	0.29	−3.5 (−25.2, 15.8)
Rrs20	9.4	8.2	0.19	−1.8 (−14.4, 19.0)	13.4	0.35	−9.3 (−36.1, 20.1)§
DRrs5-Rrs20	26.0	35.7	0.21	−3.4 (−38.2, 144.4)	30.2	0.44	25.1 (−23.7, 284.8)§
Xrs5	22.6	25.9	0.22	3.1 (−26.1, 41.1)	26.9	0.28	7.1 (−42.0, 80.0)
Xrs10	21.9	16.3	0.11	0 (−36.0, 33.3)	18.1	0.21	11.7 (−25.0, 112.2)
Xrs15	41.7	25.1	0.13	0 (−47.1, 80.0)	22.0	0.16	0 (−37.9, 100.0)
Xrs20	62.6	47.0	0.10	0 (−98.0, 86.7)	54.3	0.13	−8.3 (−81.0, 200.0)
Fres	7.4	6.6	5.50	−0.6 (−22.2, 3.2)‡	6.4	7.34	−4.9 (−26.0, 13.4)‡
AX	20.8	22.3	2.12	−3.8 (−38.1, 27.8)‡	16.7	2.77	1.5 (−38.6, 90.7)

* Data in each cell correspond to the population's average.
† Data in each cell correspond to the population's median and to 5th and 95th percentiles (in parentheses).
‡ $P < .05$ vs baseline values (Wilcoxon signed-rank test with Bonferroni correction).
§ $P < .01$ vs baseline values (Wilcoxon signed-rank test with Bonferroni correction).
IOS = impulse oscillometry system
im-CV = intrameasurement coefficient of variability (100*standard deviation/mean, expressed in percentage)
CR = coefficient of repeatability ($CR = 1.96 \times \sqrt{\Sigma(x_1 - x_2)^2/(n - 1)}$), expressed in the same units of the respective IOS variable
Zrs = respiratory system impedance, followed by the frequency at which measured (5, 10, 15, or 20 Hz), all expressed in kPa/L/s
Rrs = respiratory system resistance, followed by the frequency at which measured (5, 10, 15, or 20 Hz), all expressed in kPa/L/s
DRrs5 − Rrs20 = difference of Rrs5 minus Rrs20, in kPa/L/s
Xrs = respiratory system reactance, followed by the frequency at which measured (5, 10, 15, or 20 Hz), all expressed in kPa/L/s
Fres = resonant frequency, in Hz
AX = area of reactance, in kPa/L

Table 4. Spearman's Correlation Coefficients Between Anthropometric and IOS Variables in 283 Healthy Children and Adolescents

IOS Variable	Spearman's Correlation Coefficients		
	Age	Weight	Height
Zrs5	−0.88	−0.84	−0.88
Zrs10	−0.89	−0.84	−0.88
Zrs15	−0.87	−0.84	−0.87
Zrs20	−0.85	−0.81	−0.85
Rrs5	−0.87	−0.83	−0.87
Rrs10	−0.88	−0.83	−0.88
Rrs15	−0.87	−0.83	−0.87
Rrs20	−0.85	−0.81	−0.85
DRs5-Rrs20	−0.67	−0.62	−0.66
Xrs5	0.80	0.77	0.80
Xrs10	0.79	0.74	0.78
Xrs15	0.76	0.72	0.76
Xrs20	0.77	0.73	0.77
Fres	−0.74	−0.70	−0.74
AX	−0.82	−0.77	−0.81

IOS = impulse oscillometry system
Zrs = respiratory system impedance, followed by the frequency at which measured (5, 10, 15, or 20 Hz), all expressed in kPa/L/s
Rrs = respiratory system resistance, followed by the frequency at which measured (5, 10, 15, or 20 Hz), all expressed in kPa/L/s
DRrs5 − Rrs20 = difference of Rrs5 minus Rrs20, in kPa/L/s
Xrs = respiratory system reactance, followed by the frequency at which measured (5, 10, 15, or 20 Hz), all expressed in kPa/L/s
Fres = resonant frequency, in Hz
AX = area of reactance, in kPa/L

from $r_S = -0.62$ to $r_S = -0.89$ (Table 4). In nearly all cases, regression analyses corroborated that better straight-line fitting (greater coefficients of determination) was achieved when data values were transformed into the respective $\log_{10}$ (age) or reciprocal (height and weight) values, as exemplified in Figure 1; thus, this data transformation was used in subsequent analyses. In the majority of regression analyses, 1 or 2 outliers were deleted, excepting for Fres and AX, where up to 6 outliers were eliminated. Through pairwise comparison of regression lines, small differences could be detected between males and females, either in their slopes and/or in their intercepts (see the supplementary figures at http://www.rcjournal.com). Because these differences achieved or were very close to achieving statistical significance, especially in Xrs, all reference values were evaluated separately by gender.

Multiple linear regression analysis identified height as the most influential variable in the majority of IOS variables, but age also accounted for a moderate-to-large influence in the regression models of many IOS variables, whereas body weight was excluded from nearly all of the regression models; thus, reference values were constructed considering age and height. The only exception was DRrs5 − Rrs20, because this variable achieved its highest correlation with age (without $\log_{10}$ transformation), and height did not improve the model; therefore, equation for this variable was a straight-line regression. The final equa-

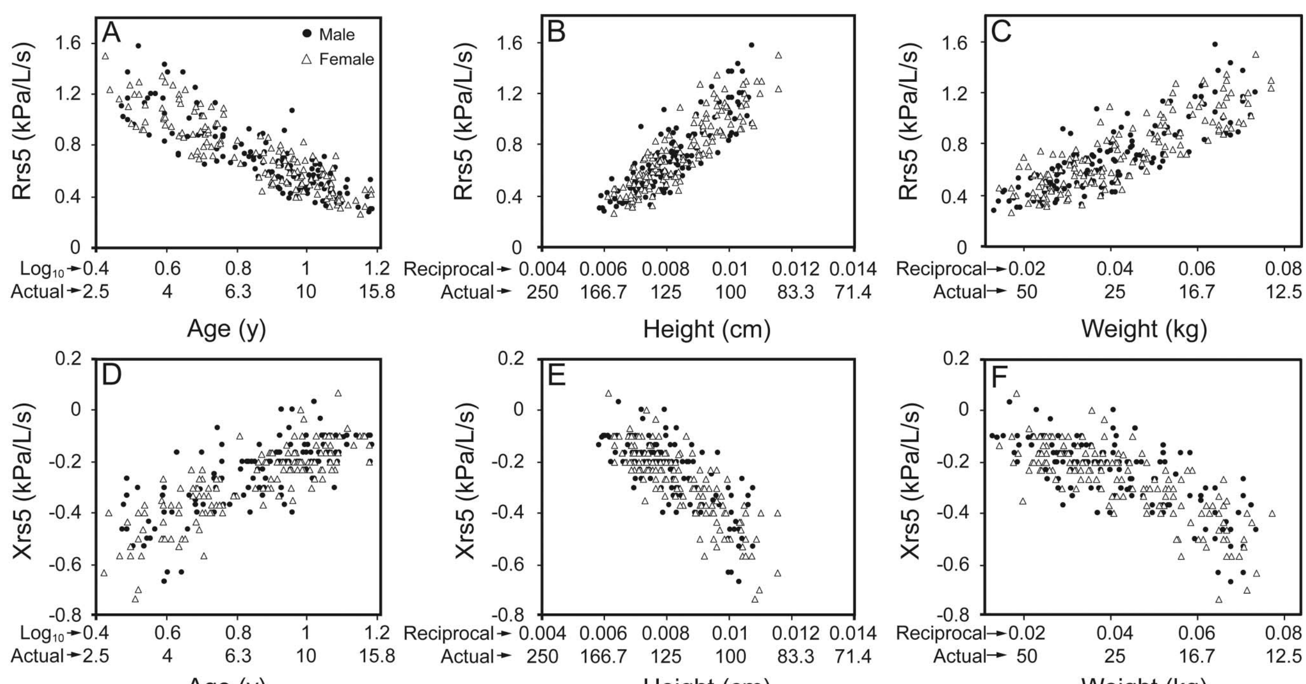

Fig. 1. Association of selected impulse oscillometry variables with age, height, and weight in a population of 283 healthy children and adolescents. Data corresponding to x-axes were transformed into the respective $\log_{10}$ (age) or reciprocal (height and weight) values to yield better linearity. Symbols correspond to male (filled circles) and female (empty triangles) subjects.

Table 5. Equations for Calculating Reference Values of IOS Variables in 130 Healthy Male Children and Adolescents

IOS Variable	A (Age Coefficient)	B (Height Coefficient)	C (Constant)	r	RSD
Zrs5	−0.694*	107.856*	0.476	−0.87	0.1494
Zrs10	−0.622*	78.317†	0.514	−0.87	0.1188
Zrs15	−0.484*	86.227*	0.268	−0.88	0.1051
Zrs20	−0.377†	82.941*	0.148	−0.87	0.0974
Rrs5	−0.636*	99.506*	0.443	−0.86	0.1405
Rrs10	−0.590*	75.807†	0.488	−0.87	0.1146
Rrs15	−0.462*	83.927*	0.254	−0.88	0.1012
Rrs20	−0.367†	82.162*	0.140	−0.87	0.0965
DRrs5-Rrs20	−0.0218*	NA	0.3864	−0.60	0.0928
Xrs5	0.228	−46.787†	−0.068	0.79	0.0784
Xrs10	0.209†	−20.758	−0.145	0.72	0.0613
Xrs15	0.208†	−19.108	−0.121	0.73	0.0587
Xrs20	0.170†	−19.298	−0.019	0.80	0.0419
Fres	−11.675†	958.724	24.027	−0.74	3.0244
AX	−3.938†	340.493	2.635	−0.78	0.9094

Each equation corresponds to: IOS variable = A × (log of age in years) + B × (1/height in cm) + C, excepting DRrs5 − Rrs20 = A × (age in years) + C. The z score for an individual subject can be calculated through the formula: z score = (observed value − predicted value)/RSD.
* $P < .01$.
† $P < .05$.
IOS = impulse oscillometry system
RSD = standard deviation of residuals
r = correlation coefficient
Zrs = respiratory system impedance, followed by the frequency at which measured (5, 10, 15, or 20 Hz), all expressed in kPa/L/s
Rrs = respiratory system resistance, followed by the frequency at which measured (5, 10, 15, or 20 Hz), all expressed in kPa/L/s
DRrs5 − Rrs20 = difference of Rrs5 minus Rrs20, in kPa/L/s
NA = not applicable
Xrs = respiratory system reactance, followed by the frequency at which measured (5, 10, 15, or 20 Hz), all expressed in kPa/L/s
Fres = resonant frequency, in Hz
AX = area of reactance, in kPa/L

Table 6. Equations for Reference Values of IOS Variables in 153 Healthy Female Children and Adolescents

IOS Variable	A (Age Coefficient)	B (Height Coefficient)	C (Constant)	r	RSD
Zrs5	−0.595*	130.320*	0.214	−0.90	0.1374
Zrs10	−0.608*	88.681*	0.428	−0.90	0.1107
Zrs15	−0.487*	85.634*	0.285	−0.90	0.1020
Zrs20	−0.474*	69.140*	0.361	−0.88	0.0980
Rrs5	−0.736*	78.861*	0.702	−0.89	0.1221
Rrs10	−0.579*	80.283*	0.450	−0.91	0.1004
Rrs15	−0.502*	74.631*	0.376	−0.89	0.0995
Rrs20	−0.427*	69.880*	0.307	−0.89	0.0907
DRrs5-Rrs20	−0.0229*	NA	0.3866	−0.65	0.0861
Xrs5	0.309*	−42.906†	−0.185	0.85	0.0709
Xrs10	0.220†	−23.295	−0.139	0.80	0.0544
Xrs15	0.147	−31.523†	0.041	0.79	0.0541
Xrs20	0.072	−31.781*	0.168	0.79	0.0423
Fres	−0.308	2542.196*	0.791	−0.76	2.8344
AX	−2.345	640.548*	−1.212	−0.83	0.8207

Each equation corresponds to: IOS variable = A × (log of age in years) + B × (1/height in cm) + C, excepting DRrs5 − Rrs20 = A × (age in years) + C. The z score for an individual subject can be calculated through the formula: z score = (observed value − predicted value)/RSD.
* $P < .01$.
† $P < .05$.
IOS = impulse oscillometry system
RSD = standard deviation of residuals
r = correlation coefficient
Zrs = respiratory system impedance, followed by the frequency at which measured (5, 10, 15, or 20 Hz), all expressed in kPa/L/s
Rrs = respiratory system resistance, followed by the frequency at which measured (5, 10, 15, or 20 Hz), all expressed in kPa/L/s
DRrs5 − Rrs20 = difference of Rrs5 minus Rrs20, in kPa/L/s
NA = not applicable
Xrs = respiratory system reactance, followed by the frequency at which measured (5, 10, 15, or 20 Hz), all expressed in kPa/L/s
Fres = resonant frequency, in Hz
AX = area of reactance, in kPa/L

tions for males and females are shown in Tables 5 and 6, respectively.

In Figure 2, the curvilinear regression lines obtained in the present study were compared with already published reference equations in other populations.

Discussion

In the present study, a set of reference values for each IOS variable was obtained in a population of healthy children and adolescents. As occurs with other pulmonary function tests, we found that IOS values progressively changed as children grew up. In many of the published IOS reference equations, such as those proposed by Park et al,[12] Lee et al,[13] Hellinckx et al,[14] and Frei et al,[15] the relationship between IOS variables and anthropometric parameters such as height was found to follow a straight-line fitting. This is in contrast with our results, in which a curvilinear fitting was observed, and might be explained by the narrower age range studied by these authors (up to the age of 10 y). However, in the study by Dencker et al[16] with a maximum age of 11 y in their study population, a curvilinear association between height and IOS was found, and this curvilinear fit was more accentuated in the study by Nowowiejska et al,[17] who, in their analysis, included subjects up to 19 y of age. The downward trend of Rrs as age advances could be explained by progressive widening of the tracheobronchial tree during childhood, which is expected to stabilize in early adulthood.

Our study fully agrees with those of other authors concerning the utmost relevance of height in determining IOS values.[12,13,15-17] Only a few studies have included in their reference equations additional anthropometric variables such as age[13] and weight,[16] probably due to the obvious colinearity between these variables. However, through multivariate analysis, we found that, in the majority of IOS indices, a better fit was achieved by introducing age into the regression model; thus, this variable was also used in the final equations. Independently from height, the addi-

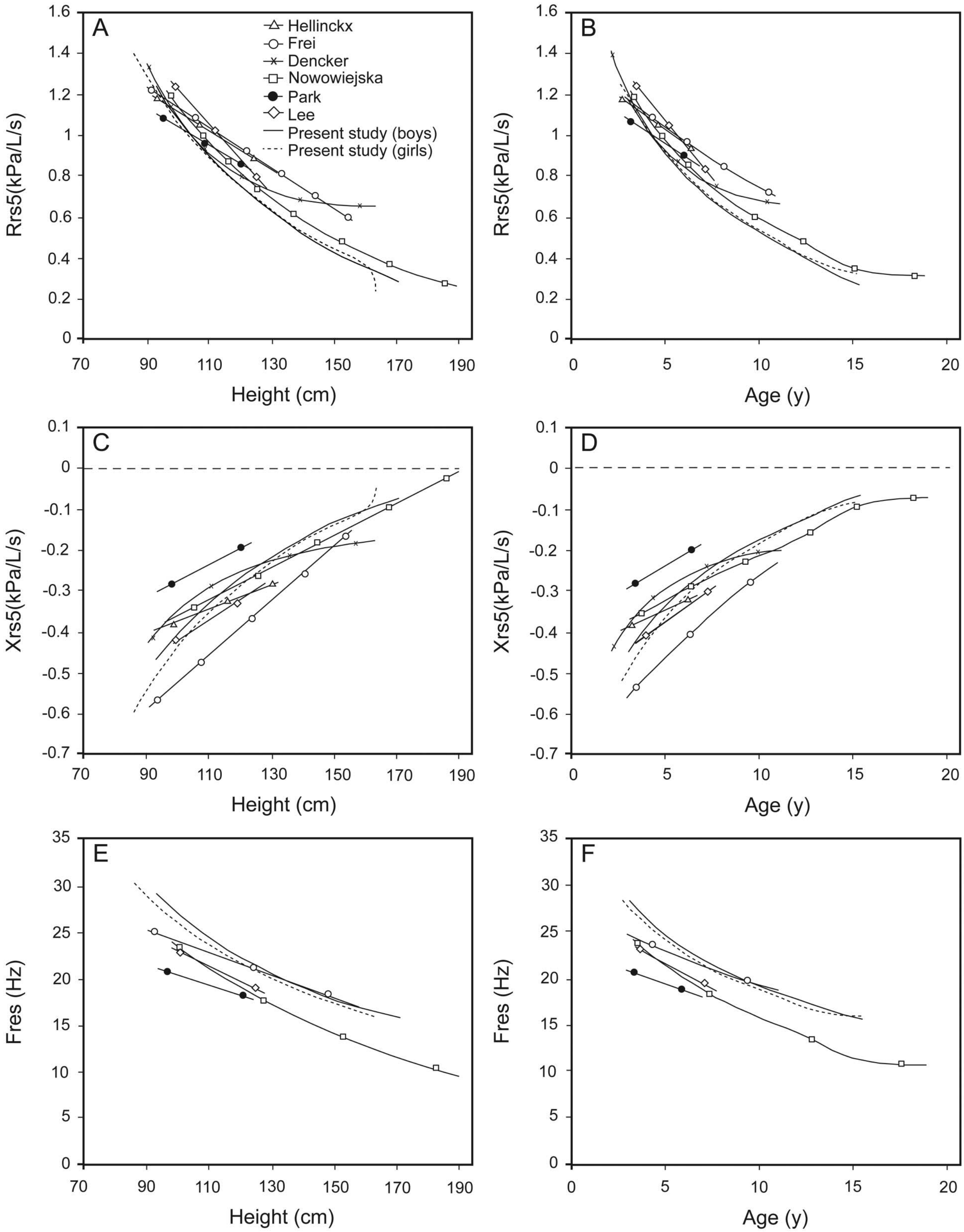

Fig. 2. Regression lines for boys and girls obtained in the present study and those already reported by several authors (for both genders). The ideal (50th percentile) height-for-age and weight-for-age published by the Centers for Disease Control and Prevention were used in those equations including more than one anthropometric variable. Note that, according to our regression lines, when adolescent girls attain their final adult height (around 163 cm), age then becomes the more relevant influence, causing further modifications in respiratory system resistances (Rrs5) and reactances (Xrs5) at 5 Hz (A and C, respectively).

tional mechanism by which age can modify lung function is not clear, but it must be kept in mind that, once adult height is reached by the subject, the main variable determining further changes in lung function is age.

Our results indicated that subtle differences existed in several IOS variables between males and females; thus, the sets of reference values were calculated separately for each gender. In previous studies, Park et al[12] and Nowowiesjka et al[17] also presented reference values for boys and girls separately, although no mention was made concerning how large or how close to statistical significance those differences were. In our study, this slight gender difference was more noticeable in older subjects in the case of respiratory resistances, and in the younger population for respiratory reactances (as observed in the supplementary materials at http://www.rcjournal.com). According to our results, adolescent girls tended to have greater respiratory resistance than adolescent boys. Some studies have shown that respiratory resistances in adults are greater in women, as compared with men,[18,19] and thus it is possible that adolescence constitutes the age at which these gender differences in lung function are being established.

In agreement with most published studies, we found high intrameasurement variability in some IOS variables, especially Xrs, AX, and DRrs5 − Rrs20. The physiological basis of this variability remains unclear, but it may be related with rapid changes in neural control of airway caliber, as we have proposed previously for the high variability of airway resistance measured by the interrupter technique.[20] On the other hand, evaluation of short-term variability showed that Rrs and Zrs had a tendency to be lower in the second IOS measurement obtained 30 min after the first maneuver. It is known that stressful tasks such as speaking in public, performing a school examination, or viewing unpleasant scenes give rise to an increased respiratory resistance, mainly in central airways.[21,22] Thus, it is possible that the emotional stress produced by the first IOS procedure itself was accompanied by a mild degree of airway obstruction, which was partially alleviated in the second IOS maneuver. The further lowering of Rrs20 after 15 days could well reflect a much lower degree of stress in the subject. Finally, it must be noted that, in our study, the increased values of DRrs5 − Rrs20 observed at day 15 were due to this lowering of Rrs20 and not to an increase of Rrs5, which was stable. This is relevant because an increment of DRs5-Rs20 has been proposed to be indicative of heightened peripheral airway resistance,[23-25] and, as our study suggests, this is not always true, because a relevant decrease of central airways resistance could also modify DRrs5 − Rrs20 in the same direction.

A consensus panel on pulmonary function tests recommended that, in a given subject, IOS results be reported as a z score, a value that indicates how many standard deviations the individual is below or above the predicted mean for any given parameter.[9] In our reference population, once the multivariate regression was constructed for each IOS variable, the residual or error of each value was calculated with the difference between observed and predicted values. The standard deviation of these residuals (RSD), which closely reflects the standard error of the regression, can be used to calculate the z score of an individual subject through the formula $z = (\text{observed value} - \text{predicted value})/\text{RSD}$.

Conclusions

In the present study, we obtained equations for calculating the reference values of each IOS variable. All IOS variables were strongly associated with height; however, in many of these, age also greatly influenced the result. Hence, both anthropometric variables were introduced into the equations. Although these reference values were obtained in a population of Mexican children and adolescents, it is probable that our results can be also applicable to other Latin American populations sharing the same ethnic background.

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