Lung Function Reference Values in Children and Adolescents Aged 6 to 18 Years in Galicia

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OBJECTIVE: It is well known that lung function reference values differ between populations, hence the apparent importance of establishing such values. The aim of this study was to develop prediction equations for spirometry for healthy children and adolescents in Galicia, Spain.

POPULATION AND METHODS: We studied children and adolescents aged 6 to 18 years from randomly selected schools in 14 municipalities in Galicia. Spirometric values were measured following the protocols established by the American Thoracic Society in 1987, with real-time monitoring of flow-volume curves. The prediction equations were derived using multivariate linear regression.

RESULTS: We developed equations to predict the main spirometry parameters for this age group according to sex, height, and weight. Mean spirometry values in relation to height were higher for boys than for girls, except in the 140-160 cm range, where they were higher for girls. Equations published in other studies in similar populations gave different predictions, ranging from an underestimation of forced midexpiratory flow rate ($FEF_{25\%-75\%}$) by 16% in comparison to ours to an overestimation of peak expiratory flow (PEF) rate by 15% for an average boy. For a girl, the corresponding differences ranged from an underestimation of $FEF_{25\%-75\%}$ by 17% to an overestimation of PEF by 19%.

CONCLUSIONS: These results support the importance of using population-specific prediction equations to establish lung function reference values.

Key words: *Spirometry. Healthy children. Reference values.*

Valores de referencia de función respiratoria en niños y adolescentes (6-18 años) de Galicia

OBJETIVO: Son conocidas las diferencias entre distintas poblaciones en cuanto a los valores de referencia de la función respiratoria, por lo cual parece importante establecerlos. El objetivo del estudio ha sido establecer las ecuaciones de predicción de parámetros espirométricos en niños y adolescentes sanos de Galicia.

POBLACIÓN Y MÉTODOS: Hemos estudiado a niños y adolescentes sanos de 6 a 18 años de edad, de colegios seleccionados aleatoriamente en 14 municipios de Galicia. Las maniobras espirométricas se realizaron de acuerdo con los protocolos de la American Thoracic Society de 1987, con evaluación continua de los espirogramas. Se obtuvieron las ecuaciones de predicción mediante regresión lineal multivariante.

RESULTADOS: Con este estudio se obtuvieron las ecuaciones de predicción de los principales parámetros espirométricos en este grupo de edad, en función de la edad, el sexo, la talla y el peso. Los valores medios de los parámetros espirométricos, en función de la estatura, son superiores en la población masculina comparada con la femenina, excepto en el rango entre 140 y 160 cm de altura, donde las mujeres superan a los varones. Para un varón medio de nuestra población, los parámetros de función pulmonar obtenidos con las ecuaciones de predicción referidas por otros autores en poblaciones similares difieren de los nuestros, desde una infraestimación de un 16% para el flujo mesoespiratorio forzado hasta una sobreestimación de un 15% para el pico de flujo espiratorio; para una mujer, las discrepancias van desde la infraestimación del flujo mesoespiratorio forzado del 17% hasta la sobreestimación del pico de flujo espiratorio de un 19%.

CONCLUSIONES: Estos resultados refuerzan la importancia de utilizar ecuaciones de predicción específicas para cada población.

Palabras clave: *Espirometría forzada. Niños sanos. Valores de referencia.*

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Introduction

Lung function is known to differ from one population to the next in accordance with a variety of factors such as climate, environmental pollution, socioeconomic conditions, and race. These factors can have a direct or indirect effect on lung function as they, in turn, influence other variables such as anthropometric features, nutritional status, and muscle strength. It is therefore important to establish lung function reference values for each community.[1-7]

Moreover, because reference values for children and adolescents are generally based on height (although other variables such as age and weight are also common), these values should be revised at least once for every new generation as anthropometric characteristics vary from one generation to the next.[8] Height gain due to an increase in leg length rather than in chest length from one generation to the next, for example, would tend to lead to a reduction in lung function within the same height category.[1] This is why reference values based on height measured with the subject in a sitting position are more accurate, albeit less common.[9,10]

The aim of the present study was to develop lung function prediction equations for healthy children and adolescents in Galicia, Spain. We also report means and percentiles for the most common spirometric values that are measured in this age group. The study formed part of the Galinut study, which analyzed diet, lifestyle, and respiratory and cardiovascular health in children and adolescents from Galicia.[11]

Population and Methods

Population

A cross-sectional study was performed in children and adolescents aged 6 to 18 years in Galicia. We chose 14 of the 315 municipalities in Galicia at random, and in each of these municipalities a school with children aged between 6 and 18 years was then chosen at random. We included all the students in the participating schools whose parents or guardians gave their informed consent and completed the study questionnaire (see Data Collection section). We excluded students who did not complete the lung function tests correctly, who reported being active smokers (not counting an occasional cigarette), who had allergic diseases, who had been hospitalized with a respiratory or cardiovascular complaint, or who did not fulfill the GAP conference committee criteria for healthy children.[12]

The final sample included 2404 children and adolescents (1268 males and 1136 females), representing approximately 0.8% of the total population of this age group in Galicia. The reproducibility of the distribution of the population in terms of age and sex was acceptable.

Written informed consent was obtained from all the children's parents or guardians prior to the completion of the questionnaires and tests. The study was approved by the ethics committee of Galicia.

Data Collection

A week prior to the tests, the research team informed the students and their parents or guardians about the characteristics of the study. This information was communicated in person at the school and by letter. Parents or guardians were sent a questionnaire asking about past and present diseases, lifestyle habits, and smoking (both student and parents). (Students over the age of 10 years were also asked privately about their smoking habits.) When the questionnaire was returned, the research team resolved any doubts that had emerged.

Individuals were weighed in their underwear and socks to an accuracy of ±0.5 kg and height was measured to an accuracy of ±0.5 cm using a stadiometer. The subjects were placed with their backs to a vertical rod, their feet forming an angle of 60º and their heels touching the base of the rod. Their shoulder blades and head were also made to touch the vertical rod with the head positioned in the Frankfurt plane.

Two physicians previously trained at our hospital's pediatric respiratory medicine clinic conducted the lung function tests during school hours, between 9:00 AM and 1:00 PM in all cases. The tests were performed using a portable spirometer (Datospir 92; Sibel SA, Barcelona, Spain) fitted with a Fleisch-type pneumotachometer. Volume calibration was semiautomatic and flow-volume curves were processed and validated by computer in real time.

The spirometer was calibrated every morning prior to testing using a 3-L syringe and 3 injections at different speeds. Two members of the research team served as biological controls. The semiautomatic calibration program had a guaranteed error rate of less than 1% for the 3-L volume calibration procedure. Room temperature, barometric pressure, and relative humidity were all measured prior to calibration.

The lung function tests were performed in accordance with the protocols established by the American Thoracic Society (ATS).[13] The subject, wearing a nose clip, was seated and performed a minimum of 3 and a maximum of 8 maneuvers. The start of the spirometry test was estimated using back-extrapolated volume (less than 0.15 L or 5% of forced vital capacity [FVC]). Other acceptability criteria included a smooth curve with an abrupt start and a positive deflection, expiration lasting at least 6 seconds, and a plateau in the volume-time curve (change in volume of less than 40 mL for at least 2 seconds). FVC and forced expiratory volume in 1 second (FEV_1) were considered acceptable when the difference between the best 2 valid maneuvers was less than 200 mL. Finally, the best FVC and FEV_1 values obtained from valid curves were chosen and the other study parameters were calculated using the maneuver with the best combined FVC and FEV_1 values.

Statistical Analysis

The *t* test and χ^2 test were used to compare means and the Kolmogorov-Smirnov test to determine whether variables were normally distributed. Prediction equations were calculated separately for each sex using stepwise multiple logistic regression. Logarithmic transformation was applied to the following spirometric parameters: FVC, FEV_1, FEV_1/FVC, peak expiratory flow (PEF), and forced midexpiratory flow rate ($FEF_{25\%-75\%}$). As predictor variables, we used age, weight, height, and their corresponding squares. We also analyzed other statistics for these variables to determine the final model, using conventional stepwise regression analysis. The statistics analyzed were coefficient of determination (R^2), residual SD, distribution of residuals, and homogeneity of variances.

Because height had the greatest predictive power in all the multiple regression analyses, we derived the spirometric parameters in relation to height only using the Lowess method.[14] The smoothed percentile curves derived for the spirometric parameters in function of height were adjusted using the LMS method described by Cole et al[15] to normalize the distribution of data for each age group using smoothed Box-Cox transformation.

Results

We studied 2404 children and adolescents, 53% of whom were boys. Table 1 shows the distribution of the study population by age and sex. The mean ages were 12.9 years for boys and 12.7 years for girls; the mean heights were 156.1 cm for boys and 150.3 cm for girls. Table 2 shows

TABLE 1
Study Population by Sex and Age

Age, y	No. of Boys	No. of Girls	Total, No.
6	30	37	67
7	50	45	95
8	60	60	120
9	93	88	181
10	98	86	184
11	93	81	174
12	122	101	223
13	89	85	174
14	151	130	281
15	181	158	339
16	160	139	299
17	88	81	169
18	53	45	98
Total, No.	1268	1136	2404

the characteristics of the study population (age, height, weight, and lung function parameters).

The spirometric parameters were subjected to logarithmic transformation because they were nonnormally distributed.

Table 3 shows the results of the multiple regression analyses for both sexes, together with the prediction equations for the different lung function parameters. The spirometric parameters were presented as dependent variables in relation to height, weight, and age, and their corresponding squares. The R^2 values were within the range of 0.80 to 0.90 for the model with the best fit for FVC and FEV_1 and within 0.61 and 0.71 in the case of PEF and $FEF_{25\%-75\%}$. The natural logarithm (FEV_1/FVC) had practically no correlation with any of the independent variables analyzed, unsurprisingly given the inherent correlation between FEV_1 and FVC.

TABLE 2
Characteristics of Study Population

	Mean	Median	Interquartile Range	Minimum–Maximum
Boys (n=1268)				
Age, y	12.9	13	10-15	6-18
Weight, kg	49.1	50	35-63	16.5-93
Height, cm	156.1	159	142.2-171.0	110.7-188.8
BMI, kg/m^2	19.4	19.3	16.9-21.6	11.6-30.0
FVC, L	3.42	3.32	2.34-4.45	0.99-7.92
FEV_1, L	3.08	2.99	2.13-4.01	0.93-6.87
FEV_1/FVC, %	90.9	91.5	87.3-95.5	70.6-99.8
PEF, L/min	371.7	353.4	255.0-471.0	62.4-899.4
$FEF_{25\%-75\%}$, L/s	3.75	3.58	2.62-4.800	0.62-8.28
Girls (n=1136)				
Age, y	12.7	13	10-15	6-18
Weight, kg	45.3	48	35-55	17.0-82.0
Height, cm	150.3	154.5	140.5-160.7	110.0-179.5
BMI, kg/m^2	19.6	19.6	17.3-21.7	11.2-30.0
FVC, L	2.82	2.92	2.19-3.45	0.910-5.880
FEV_1, L	2.61	2.75	1.97-3.19	0.760-4.570
FEV_1/FVC, %	92.6	93.7	89.1-97.1	70.6-99.7
PEF, L/min	297.45	298.20	224.4-361.8	84.0-576.0
$FEF_{25\%-75\%}$, L/s	3.40	3.41	2.3-4.22	0.690-6.540

Abbreviations: BMI, body mass index; $FEF_{25\%-75\%}$, forced midexpiratory flow rate; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; PEF, peak expiratory flow.

TABLE 3
Lung Function Prediction Equations for Children and Adolescents in Galicia

Equation	R^2	RSD
Boys		
$\log_e$ (FVC) =–1.230 + 0.01106H + 0.03278A + 0.004881W	0.89	0.13153
$\log_e$ (FEV_1) = –1.217 + 0.01073H + 0.001252A^2 + 0.01084W – 0.0000572W^2	0.90	0.11820
$\log_e$ (PEF) = 3.730 + 0.007H + 0.040A + 0.014W –0.000085W^2	0.71	0.21890
$\log_e$ ($FEF_{25\%-75\%}$) = –0,528 + 0.006839H + 0.001609A2 + 0.01230W – 0.0000672W^2	0.67	0.22823
$\log_e$ (FEV1/FVC) = 4.522 –0.00000519W^2	0.02	0.06673
Girls		
$\log_e$ (FVC) = –1.511 + 0.009143H + 0.09124A + 0.01174W – 0.00244A^2 – 0.0000664W^2	0.81	0.14316
$\log_e$ (FEV_1) = –1.664 + 0.009283H + 0.09805A + 0.01273W – 0.00275A^2 – 0.0000771W^2	0.85	0.12490
$\log_e$ (PEF) = 3.128 + 0.008H + 0.159A – 0.005A^2 + 0.005W	0.61	0.21779
$\log_e$ ($FEF_{25\%-75\%}$) = –1.147 + 0.007087H + 0.136A – 0.00402A^2 + 0.004496W	0.61	0.22108
$\log_e$ (FEV_1/FVC) = 4.539 – 0.0000699A^2	0.01	0.06161

Abbreviations: A, age, y; $FEF_{25\%-75\%}$, forced midexpiratory flow rate, L/s; FEV_1, forced expiratory volume in 1 second, L; H, height, kg; FVC, forced vital capacity, L; $\log_e$, natural logarithm; PEF, peak expiratory flow, L/min; R^2, coefficient of determination; RSD, residual SD.

TABLE 4
Comparison of Spirometric Parameters Predicted for the Study Population With Those Reported by Other Authors and Percentage Differences

Authors	FVC		FEV_1		PEF[a]		$FEF_{25\%-75\%}$	
	mL R^2	Difference	mL R^2	Difference	L/s R^2	Difference	L/s R^2	Difference
Boys								
Present study	3192		2893		5884		3498	
	0.89		0.90		0.71		0.67	
Pérez-Padilla et al[16]	3515	+10%	3072	+6%	6765	+15%	3637	+4%
	0.89		0.89		0.79		0.65	
Manzke et al[17]	3244	+2%	2872	–1%	6055	+3%	3127	–11%
	0.92		0.93		0.86		0.74	
Hankinson et al[3] (white Americans)	3337	+4%	2908	0	6092	+3%	3243	–7%
	0.87		0.85		0.78		0.56	
Hankinson et al[3] (Mexican Americans)	3461	+8%	3027	+5%	6308	+7%	3532	+1%
	0.86	0.85	0.85		0.75		0.55	
Wang et al[7] (white population)	3081	–4%	2644	–9%			2923	–16%
Rosenthal et al[18]	3073	–4%	2563	–11%	5408	–8%		
	0.98		0.99		0.98			
Chinn and Rona[19]	3102	–3%	2686	–7%			2969	–15%
	0.69		0.65				0.25	
Casan[20]	3598	+13%	3008	+4%	6195	+5%	3418	–2%
	0.90		0.89		0.82		0.69	
Coultas et al[21]	3239	+1%	2825	2%	6020	+2%	3234	–8%
	0.91		0.91	-	0.81		0.72	
Sanz Ortega et al[22,23]	3146	–1%	2759	–5%			3602	+3%
	0.83		0.82				0.43	
Morato Rodríguez et al[24]	3171	–1%	2661	–8%				
	0.89		0.87					
Trabelsi et al[25]	3087	–3%	2689	–7%	5703	–3%	3040	–13%
	0.90		0.89		0.87		0.74	
Girls								
Present study	2796		2599		4966		3343	
	0.81		0.85		0.61		0.61	
Pérez-Padilla et al[16]	2928	+5%	2621	+1%	5911	+19%	3438	+3%
	0.83		0.83		0.70		0.57	
Manzke et al[17]	2914	+4%	2657	+2%	5592	+13%	3023	–10%
	0.91		0.93		0.84		0.75	
Hankinson et al[3] (white Americans)	2894	+3%	2565	–1%	5609	+13%	3279	–2%
	0.73		0.75		0.56		0.50	
Hankinson et al[3] (Mexican Americans)	2930	+5%	2614	+1%	5685	+14%	3400	+2%
	0.71		0.73		0.47		0.43	
Wang et al[7] (white population)	2674	–4%	2398	–8%			2990	–11%
Rosenthal et al[18]	2566	–8%	2240	–14%	5060	+2%		
	0.98		0.99		0.97			
Chinn and Rona[19]	2663	–5%	2374	–9%			2930	–12%
	0.67		0.64				0.30	
Casan[20]	2994	+7%	2581	–1%	5122	+3%	3263	–2%
	0.88		0.88		0.77		0.62	
Coultas et al[21]	2670	–5%	2347	–10%	4868	–2%	2784	–17%
	0.86		0.84		0.65		0.52	
Sanz Ortega et al[22,23]	2691	–4%	2327	–11%			3718	+11%
	0.83		0.83				0.54	
Morato Rodríguez et al[24]	2656	–5%	2451	–6%				
	0.89		0.87					
Trabelsi et al[25]	2666	–5%	2361	–9%	4857	–2%	2921	–13%
	0.89		0.88		0.78		0.75	

Abbreviations: $FEF_{25\%-75\%}$, forced midexpiratory flow rate; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; PEF, peak expiratory flow.
[a]Expressed in L/s instead of L/min to facilitate comparison of data between studies.

Mean spirometric values in relation to height were higher for boys than for girls, except in the 140 cm to 160 cm height range, where they were higher for girls (Figure 1). Figure 2 shows the curves for the lung function parameters studied, along with their corresponding percentiles.

Table 4 compares the results obtained using our prediction equations with those obtained using other equations in the literature.[3,16-25] It also shows the corresponding R^2 values and the percentage difference between the results of those studies and ours. The data shown for our study correspond to an average girl in our population (Table 2). We also examined the main features of the methods used and the populations included for each of the studies analyzed (Table 5).

Discussion

We calculated lung function reference values for FVC, FEV_1, $FEF_{25\%-75\%}$, and PEF in relation to age, height, and weight for healthy children and adolescents aged 6 to 18 years in Galicia. We also calculated mean values in relation to height and the 5th, 10th, 25th, 50th, 75th, 90th, and 95th distribution percentiles. Our results are from a relatively broad population sample that was selected using strict disease exclusion criteria recommended by the ATS.[13] In addition, all the flow-volume curves obtained were computer-validated in real time.

The best-fit model generated by stepwise multiple regression was obtained following logarithmic transformation of the spirometric results and using the following predictors: height, weight, and age, and their corresponding squares (Table 3). Given that the 3 predictors analyzed (height, weight, and age) are common and easy to obtain in routine clinical practice, we decided to include them all in the final equations, even though improvement

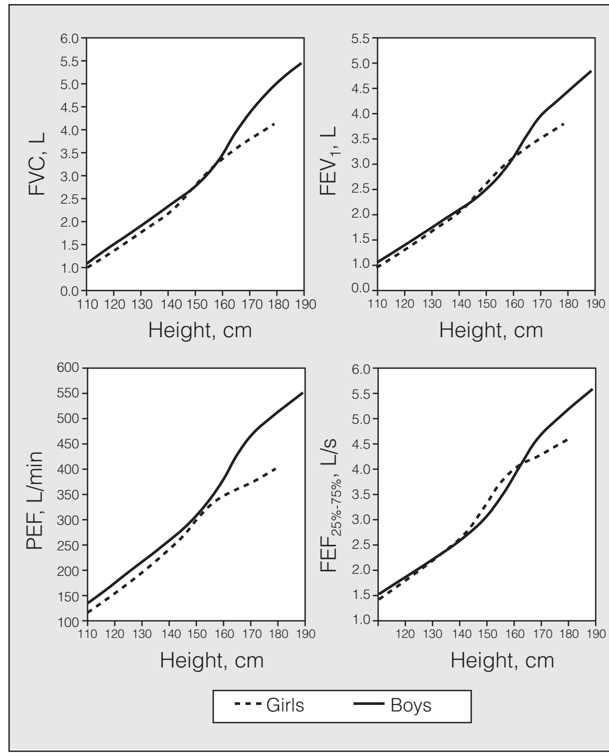

Figure 1. Mean spirometric values in relation to height, by sex. $FEF_{25\%-75\%}$ indicates forced midexpiratory flow rate; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; PEF, peak expiratory flow.

in goodness of fit was not clinically significant. It is known that lung function prediction equations based on height alone can result in under- or overestimated spirometry for the ages analyzed, particularly in the case of boys and in the youngest and oldest individuals.[26]

TABLE 5
Description of Sampling Methods Used in Studies Analyzed

Authors	Sample Size, No. of Subjects	Age Range, y	Sampling Method
Present study	1270 M 1138 F	6-18	Twice-randomized trial (towns, schools)
Pérez-Padilla et al[16]	2066 M 1943 F	8-20	Children aged 8-12 years from randomly selected schools in Mexico City and older participants from a selected school
Manzke et al[17]	213 M 187 F	6-16	White patients with psychosocial problems and skin disorders from a German rehabilitation center
Hankinson et al[3] (white Americans)	422 M 456 F	8-20	Stratified sample of general population in the USA
Hankinson et al[3] (Mexican Americans)	610 M 651 F	8-20	Stratified sample of general USA population
Wang et al[7] (white population)	11 630	6-18	Randomly selected sample from schools in 6 US cities.
Rosenthal et al[18]	455 M 317 F	4.6-18.8	White children from 12 schools in London
Chinn and Rona[19]	910 M 722 F	6.5-12.0	Representative sample of white school children in England
Casan[20]	257 M 275 F	6-20	Healthy volunteers from the metropolitan area of Barcelona (Spain)
Coultas et al[21]	151 M 177 F	6-18	All inhabitants from a randomly selected sample of homes with at least one inhabitant identified as Hispanic in a semirural town in New Mexico, USA
Sanz Ortega et al[22.23]	1156	7-14	Randomly selected sample of schools in Valencia, Spain
Morato Rodríguez et al[24]	415 M 350 F	6-14	Randomly selected sample of schools in Bilbao, Spain
Trabelsi et al[25]	581 M 533 F	6-16	Children from 10 schools in the central region of Tunisia

Abbreviations: M, males; F, females.

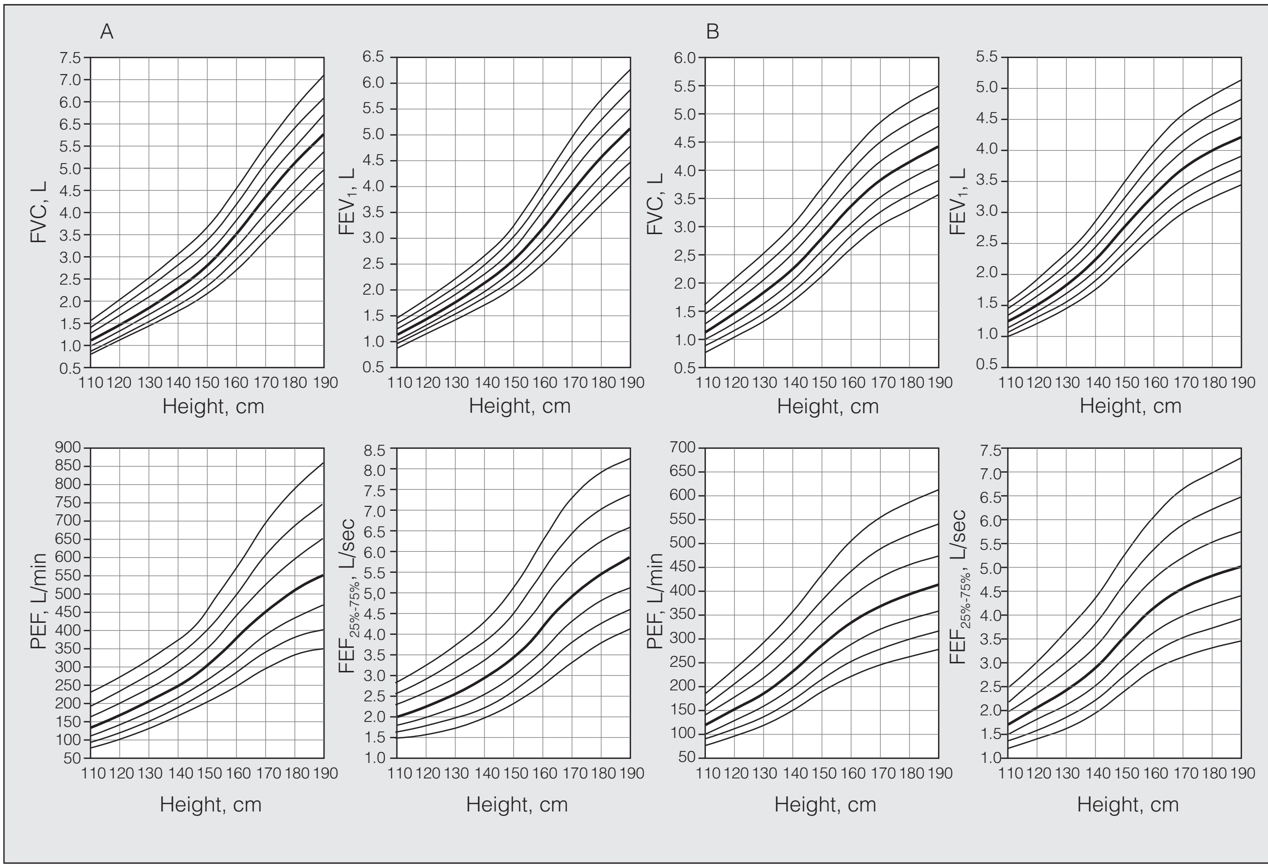

Figure 2. Smoothened lung function percentiles in relation to height, for boys (A) and girls (B). $FEF_{25\%-75\%}$ indicates forced midexpiratory flow rate; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; PEF, peak expiratory flow.

Like other authors, we found that height was the independent variable with the greatest predictive power, although in our case, the inclusion of age and weight improved the precision of predictions. In similar studies to ours conducted among children and adolescents aged 7 to 19 years and 6 to 18 years in China[27] and Singapore,[28] respectively, neither age nor weight were seen to have a significant effect on goodness of fit. In a study by Hankinson et al[3] that analyzed 3 ethnic groups aged between 8 and 20 years in the United States, height and age, but not weight, improved the predictive power of their equation. (Weight was as good a predictor as height, but it contributed little when height was already included in the equation). Height and age were the only independent variables included in studies performed in children aged 6 to 11 years in London[19] and in girls aged 6 to 16 years in Germany (PEF was added to the equation for boys).[17] A study performed in a Mexican population aged 8 to 20 years entered height, weight, and age to improve the fit of their prediction equation, just as we did.[16]

The fact that age improved the predictive power of our equations seems logical if we consider that the body and lungs mature at different rates[29,30] and that muscles continue to develop after a person has stopped growing taller. These differences in growth and development rates can affect lung function values and particularly those that depend on strength.[31,32] The fact that age exerts a different effect on lung function prediction equations in boys and girls also seems logical if we consider that the 2 sexes have different growth patterns.[17,29,31] Weight might contribute to the predictive power of spirometric equations in part because it is associated with body composition, which is known to influence lung function.[33,34] Moreover, girls' and boys' weight and height growth spurts occur at different ages and do not correspond to peaks in lung function increase.[31] Weight gain may be related to increased body fat, which in turn is related to poorer lung function. It may, however, also be related to increased muscle mass and force, which has been shown to improve certain spirometric parameters.[35,36] The above factors seem to be clearly interrelated, as lung function has been seen to improve with an increase in body mass index up to a certain point beyond which it begins to worsen.[37] The improved precision of lung function predictions following the inclusion of height, weight, and age might also be related to pubertal development as our population included pre-, peri-, and post-pubertal individuals and it is known that the onset and duration of puberty varies from one gender to the other and also from one person to the next.[38]

If we examine our results in terms of goodness of fit, they are among the best reported in the literature for FVC, FEV_1, and $FEF_{25\%-75\%}$ but among the worst for PEF

(Table 4). As in other studies,[3,17,19,20] our prediction equations were more precise for FVC and FEV_1 than for PEF and $FEF_{25\%-75\%}$, especially in girls (Table 4), a likely reflection of the greater variability of PEF and $FEF_{25\%-75\%}$.[1,39]

The differences between our results for FVC and those reported by the other authors (Table 4) ranged from –4% to 13% for boys (positive differences, 6; negative differences, 6; mean difference, 1.8%) and from –8 to 7% for girls (positive differences, 5; negative differences, 7; mean difference, –1%) . For FEV_1, the differences ranged from –11 to 6% in boys (mean, –2.9%) and from –14% to 2% in girls (mean, –5.4%). The differences were greater for PEF, ranging from –8% to 15% for boys and from –2% to 19% for girls (positive differences, 6; negative differences, 2 for both sexes); mean difference, 3% for boys and 7.5% for girls). Finally the differences for $FEF_{25\%-75\%}$ ranged from –16% to 4% in boys (mean, –6.4%) and from –17% to 11% in girls (mean, –5.1%). If we had used the equations developed by other studies to predict lung function in our population, the results would have been underestimated for most variables, with the exception of PEF. Our predicted levels for PEF were higher than those of only 3 groups: Rosental et al[18] for boys, Coultas et al[21] for girls, and Trabelsi et al[25] for both sexes. Our volume predictions were closest to those reported by Manzke et al[17] and Coultas et al for boys and by Hankinson et al[3] for girls, and our flow predictions were closest to those of Casan[20] for boys and girls and to those of Hankinson and coworkers for boys.

The differences observed between our predictions and those reported by the other studies might be due, at least in part, to differences in study populations, which included children up to 12 years,[19] 14 years,[22-24] and 16 years.[17,25] This probably means that many of the children and adolescents in the other studies analyzed were in an earlier stage of puberty than those in our study (Table 5). It is well known that pubertal growth influences lung function,[1,31] and that spirometric prediction equations developed for children and adolescents should not be extrapolated to other age groups.[40] Sample size—which in the studies analyzed ranged from 328[21] to 11 630[7]—is another factor that affects the precision of predictions.[41] The number of children and adolescents in our study (n=2408) probably lends strength to our results as our sample size is larger than those of the majority of studies conducted in similar populations (Table 5). Indeed, only 2 of the 12 studies we analyzed had a larger sample than ours. A quarter of the studies included individuals under 14 years[19,22,24] and 2 included individuals up to 16 years old.[7,25]

The parameter with the greatest mean difference between our study and the studies included in Table 4 was PEF in girls (8.8% lower in our population). This could be due to several reasons, including the fact that the girls in our study had less muscle strength or had entered puberty later than those in the other studies,[42] but this is something that we did not analyze.

As mentioned in the Results section, boys with a height of under 140 cm or over 160 cm had higher FVC, FEV_1, PEF, and $FEF_{25\%-75\%}$ values than girls. The difference was particularly significant for heights above 160 cm, likely because lung function growth ends earlier in girls than in boys. The fact that girls between 140 cm and 160 cm tall had higher spirometric values than boys in the same height range is probably due to the fact that the growth spurt occurs earlier in girls.[1,29,31,43-45]

In conclusion, we have developed prediction equations for lung function reference values for FVC, FEV_1, FEV_1/FVC, PEF, and $FEF_{25\%-75\%}$ in children and adolescents in Galicia, Spain. The differences observed between our equations and those reported in other studies seem to support the need for population-specific reference values to reduce the risk of error when interpreting test results.

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