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Ventilatory Functions in Croatian Population in Comparison with European Reference Values

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Aim. To compare ventilatory capacity of Croatian population with the ventilatory function values predicted by conventional equations based on measurements among European populations.

Methods. Ventilatory capacity and respiratory symptoms were determined in a group of 2,482 healthy non-smokers (1,162 men and 1,320 women). The measurements were performed with a pneumotach spirometer. Maximum expiratory flow volume curves (MEFV) were registered, and forced vital capacity (FVC), forced expiratory volume in one second (FEV_1), and flow rates at 50% (MEF_{50}) and the last 25% of the vital capacity (MEF_{25}) were recorded. Anthropometric data were also noted. Reference values were calculated using multiple linear regressions.

Results. Comparisons of our values with the prediction summary equations issued by the European Community for Steel and Coal (ECSC) and the European Respiratory Society (ERS) showed that healthy Croatians had consistently lower values of FVC (92.1±14.0% of the predicted volume for men and 86.2±11.7% for women) and FEV_1 (93.7±14.8% of the predicted values for men and 95.3±13.1% for women), but higher values of MEF_{50} (107.8±30.1% of the predicted values for men and 103.4±22.8% for women) and MEF_{25} (117.3±41.0% of the predicted values for men and 117.9±34.0% for women) than the ECSC/ERS recommendations. The comparison was also made with the most commonly used North American reference standards based on populations of European origin, with similar findings. On the basis of the results of multiple linear regressions, we constructed prediction equations for ventilatory function in Croatian population.

Conclusion. The ECSC/ERS recommendations are not satisfactory for the Croatian population.

Key words: *Croatia; population characteristics; pulmonary ventilation; respiratory function tests; reference values; spirometry*

In 1983, a Working party of the European Community for Steel and Coal (ECSC) issued the recommendations on reference values for ventilatory indices, designated as the "Standardization of Lung Function Tests" (1). In 1993, the ECSC and the European Respiratory Society (ERS) updated these recommendations (2).

Factors known to determine the size of the normal lung include stature, age, sex, body mass, posture, habitus, ethnic group, and daily activity pattern (3). The size of the lungs relative to body size varies with age. These measurements also vary by ethnic groups (4). Some of this variability may be due to ethnic differences, such as those characterized by trunk length relative to standing height (5). This index partly explains why black people have smaller lung volumes, with lower values for forced expiratory volume in one second (FEV_1) and forced vital capacity (FVC), but not necessarily for peak expiratory flow and other indices, than do white people with otherwise similar anthropometric measurements (4). Trunk length does not account for all the differences in the lung function between white and black populations, nor does it explain why many Indian, Polynesian, and other Asian people also have relatively small lungs (3). However, ethnic differences in alveolar size or airway dimensions could be contributing factors (5,6). Differences between ethnic groups are thus real and need to be taken into account.

In our practice, we noticed that commonly used reference values are inadequate for some lung function parameters in Croatian people. The current study was designed to assess the validity of the ECSC/ERS recommendations in predicting values for the Croatian population. To our surprise, we found consistently smaller values for ventilatory capacity and large respiratory airways, but higher values for small respiratory airways.

Subjects and Methods

Subjects

Subjects included in our study lived in urban and rural environments. They were industrial and farm workers recruited as the control cohort for epidemiological studies on the effects of air pollution in various workplaces in Croatia (7,8). The subjects, selected according to the recommendations of American Thoracic Society (9), were lifetime non-smokers, without symptoms of lung, heart, or chest disease, which could compromise their ventilatory function. We consider Croatians as an ethnically homogenous distinct population and our study population of 2,475 Croatians (1,162 men and 1,320 women), aged 20-66 years, was considered representative of the Croatian population at large. For each subject, a symptom questionnaire based on the Medical Research Council respiratory questionnaire was completed by a trained physician (10). Anthropometric measurements included age (years) and standing height (m). The Medical Ethics Committee of the Zagreb University School of Medicine approved the study.

Ventilatory Capacity Measurements

The spirometric procedure was explained and demonstrated to each subject before measurements. The measurements were taken after a 15-minute rest period. Maximum expiratory flow-volume (MEFV) curves were recorded for each subject seated in an upright position and fitted with a noseclip. Spirometry was performed on a Pneumoscreen pneumotachograph (Jaeger, Wisbaden, Germany). Forced vital capacity (FVC), forced expiratory volume in one second (FEV_1), and maximum expiratory flow rates a 50% and the last 25% of the FVC (MEF_{50} and MEF_{25}, respectively) were read from MEFV curves.

Since it is important in pulmonary function testing to minimize the variation caused by technical factors, our study was performed with equipment and methods that adhered to current standards. The equipment had been validated before the study, to comply with ECSC and American Thoracic Society recommendations (3). Calibration was performed on a daily basis. All measurements were reported after correction of flow and volume to the normal body temperature, ambient pressure, saturated with water vapor, ie, standard BTPS values. Before starting measurements, subjects were asked to follow the instructions. Four researchers were assigned to perform the measurements. Each subject had to achieve a minimum of three acceptable blows, exhaling for at least 6 seconds to a stable expiratory flow rate. The best of the three technically MEFV curves was selected on the basis of best FVC and FEV_1, and flow rates were measured on that curve. The chosen value did not exceed the next highest value by more than 5%, or 100 mL, as recommended by the American Thoracic Society guidelines (3).

Statistical Analysis

Data were expressed as mean ± standard deviation (SD). The computed differences between the measured and predicted values (ERS values) for each lung function parameter were tested by paired t-test. Additionally, multiple linear regression method was applied to adjust for standing height and age by sex. All statistical analyses were performed with SAS statistical package (11).

Results

The mean age of men was 38 ± 11 years (range, 20-64), and the mean age of women was 37 ± 10 years (range, 20-66). The mean body height of men was 1.74 ± 0.07 m (range, 1.48-1.96), and of women it was 1.61 ± 0.06 m (range, 1.43-1.83).

Comparisons of ventilatory capacity measurements in healthy Croatians with the ECSC/ERS prediction summary equations showed consistently lower values of FVC and FEV_1 in both men and women, but higher values of MEF_{50} and MEF_{25} than those contained in the ECSC/ERS recommendations (Table 1). The differences were statistically significant for all measured indices, although smaller for women than for men, except for FVC. The differences for FEV_1 and MEF_{50} for both men and women were smaller than the differences for FVC and MEF_{25}.

We obtained similar findings when comparison was made with the most commonly used North American reference standards based on populations

Table 1. Comparison of measured ventilatory capacity tests in Croatians* compared with the European Community for Steel and Coal and the European Respiratory Society (ECSC/ERS) recommendations and other reference values derived on European descent[†]

Ventilatory parameter	Study	Men		Women	
		predicted	measured/predicted (%)	predicted	measured/predicted (%)
FVC (L):					
	our study	4.3 ± 0.6 (4.3 ± 0.9)[‡]	99.5 ± 15.0	3.1 ± 0.4 (3.1 ± 0.6)[‡]	100.2 ± 13.6
	ECSC/ERS (2)	4.7 ± 0.5	92.1 ± 14.0	3.6 ± 0.4	86.2 ± 11.7
	Smolej et al (15)	4.7 ± 0.6	90.6 ± 13.7	3.5 ± 0.4	90.8 ± 12.5
	Knudson et al (12)	4.7 ± 0.7	91.3 ± 14.0	3.3 ± 0.3	94.3 ± 13.0
	Miller et al (13)	4.9 ± 0.6	88.3 ± 13.6	3.6 ± 0.4	87.0 ± 11.9
	Crapo et al (14)	4.9 ± 0.5	86.8 ± 13.5	3.5 ± 0.4	89.4 ± 12.2
FEV_1 (L):					
	our study	3.6 ± 0.5 (3.6 ± 0.8)[‡]	99.8 ± 15.7	2.7 ± 0.3 (2.7 ± 0.5)[‡]	100.6 ± 13.8
	ECSC/ERS (2)	3.9 ± 0.5	93.7 ± 14.8	2.8 ± 0.4	95.3 ± 13.1
	Smolej et al (15)	4.0 ± 0.5	91.0 ± 14.3	2.9 ± 0.3	91.6 ± 12.7
	Knudson et al (12)	3.9 ± 0.6	93.1 ± 15.1	2.8 ± 0.3	95.4 ± 13.2
	Miller et al (13)	4.0 ± 0.5	90.0 ± 14.5	3.0 ± 0.3	89.6 ± 12.4
	Crapo et al (14)	4.1 ± 0.4	89.0 ± 14.4	3.0 ± 0.4	90.3 ± 12.4
MEF_{50} (L/s):					
	our study	5.4 ± 0.7 (5.4 ± 1.6)[‡]	99.9 ± 27.9	4.0 ± 0.3 (4.3 ± 1.0)[‡]	100.6 ± 22.1
	ECSC/ERS (2)	5.0 ± 0.5	107.8 ± 30.1	4.2 ± 0.3	103.4 ± 22.8
	Smolej et al (15)	6.0 ± 0.7	91.0 ± 25.5	4.6 ± 0.4	94.3 ± 20.8
	Knudson et al (12)	4.9 ± 0.7	110.2 ± 31.6	3.8 ± 0.3	112.6 ± 25.0
MEF_{25} (L/s):					
	our study	2.6 ± 0.5 (2.6 ± 1.0)[‡]	100.5 ± 35.1	2.2 ± 0.3 (2.2 ± 0.7)[‡]	99.6 ± 28.5
	ECSC/ERS (2)	2.2 ± 0.4	117.3 ± 41.0	1.9 ± 0.5	117.9 ± 34.0
	Smolej et al (15)	2.8 ± 0.4	91.8 ± 31.9	2.4 ± 0.3	91.9 ± 26.2
	Knudson et al (12)	2.0 ± 0.4	128.1 ± 45.3	1.7 ± 0.3	132.8 ± 39.6

*Croatians: 1,162 men, aged 38±11 years, height (m): 1.74 ± 0.07; and 1,320 women, aged 37 ± 10 years, height (m): 1.61 ± 0.06.
†Abbreviations: FVC – forced vital capacity; FEV_1 – forced expiratory volume in one second; MEF_{50} and MEF_{25} – maximum expiratory flow at 50% and last 25% of FVC, respectively.
‡Measured values in our study (in brackets); $p < 0.001$ for all differences between measured and predicted ventilatory parameters, paired t-test.

of European origin (12-14). In comparison with existing values for Croatians (15), our subjects, both men and women, had significantly lower values of all measured indices (Table 1).

Prediction equations for ventilatory function in Croatians were based on the results of multiple linear regressions (Table 2). Regression coefficients for each measured ventilatory parameter showed statistically significant differences.

Table 2. Prediction equations based on standing height (H; in meters) and age (A; in years) for non-smoking healthy Croatian men and women

Variable* (unit)	Prediction equations				
	regression equation	$R^{2\dagger}$	$F^{\ddagger}$	RSD§	1.64RSD‖
Men:					
FVC (L)	5.70H-0.034A-4.26	0.48	528.77	0.64	1.05
FEV_1 (L)	4.02H-0.036A-1.96	0.49	547.42	0.55	0.91
MEF_{50} (L/s)	3.12H-0.052A+2.03	0.17	115.69	1.47	2.41
MEF_{25} (L/s)	1.44H-0.040A+1.60	0.22	159.13	0.86	1.41
Women:					
FVC (L)	4.56H-0.024A-3.31	0.47	575.44	0.42	0.69
FEV_1 (L)	3.28H-0.024A-1.71	0.45	537.11	0.36	0.59
MEF_{50} (L/s)	1.83H-0.025A+2.27	0.08	58.84	0.93	1.53
MEF_{25} (L/s)	0.61H-0.027A+2.23	0.16	121.64	0.61	1.00

*FVC – forced vital capacity; FEV_1 – forced expiratory volume in one second; MEF_{50} and MEF_{25} – maximum expiratory flow at 50% and last 25% of FVC, respectively.
†R^2 – coefficient of determination.
‡F-test, $df_1=2$; $df_2=1{,}161$; $p<0.01$.
§RSD – residual standard deviation.
‖1.64RSD – 90% confidence interval of residual standard deviation.

Discussion

Lung function testing has evolved as a tool for physiologic studies and is a useful clinical index, widely used in assessing respiratory status in clinical and non-clinical settings (16,17). Lung function testing has become a part of routine health checkup in public health screening and respiratory, occupational, and sports medicine. The results of lung function tests are commonly interpreted with respect to reference values, ie, whether or not they are within the "normal" range (9). Our study indicated that healthy Croatians had consistently smaller FVC and FEV_1, and consistently higher MEF_{50} and MEF_{25} than those predicted by the ECSC or found among European populations of similar age and height. The differences between the values of lung function tests of Croatians and ECSC/ERS predictions were smaller for women than for men, except for FVC. It seems that women in different populations vary less than men in lung function. For example, Nigerian women showed no differences with respect to the ECSC predicted values, as opposed to Nigerian men, whose values of lung function tests were lower than those predicted by the ECSC on the basis of their anthropometrical characteristics (18).

When assessing lung function values, it is also important to take into account biologic variations (18-22). The most important host factors responsible for inter-individual variations in lung function in adults are sex (±30%), body size (±20%), and age (±8%) (12,23-26). The age range of subjects in our study was 20-66 years, whereas ECSC/ERS prediction equations apply to men and women of European descent aged 18-70 years. It has been suggested that ethnic group could be an important source of inter-individual variations in studied populations: an estimated variability due to this factor is ±10% (19,23). When compared with Caucasians of European descent, values for majority of other ethnic populations usually show smaller static and dynamic lung volumes and lower forced expiratory flow rates, but similar or higher FEV_1/FVC ratios (4,27). Castellsague et al (28) analyzed five sets of reference equations for forced spirometry reported in different studies (2,12,14, 29,30), using measurements of FVC and FEV_1 obtained by the European Community Respiratory Health Survey in Spain. They showed that discrepancies among the reference equations from different authors were unlikely to result from ethnic differences within populations of European origin. The reasons for these differences were unclear, although it was suggested that they might have been a consequence of differences in body build (23,24). However, approximately 27% of inter-individual variations still remain unexplained (23).

The differences between our results and the values for Croatians reported by Smolej-Narančić et al (15) can be explained by environmental differences related to nutrition, physical activity, air pollution, and socioeconomic factors, which are also thought to contribute to differences in lung function values (5,8,15,31). Our study population was quite similar to that investigated by Smolej-Narančić et al (15) inasmuch that both populations were Croatians and lifetime non-smokers. However, our population included industrial and farm workers, living in both urban and rural environment, and at different altitude, whereas their population was rural and lived at sea level.

The results of spirometric testing are considered clinically significant, or pathological, if measured values are 20% lower than the reference values (2). Healthy Croatians had consistently lower values of FVC and FEV_1, and higher values of MEF_{50} and MEF_{25} than those stated in the ECSC/ERS recommendations. Therefore, if values measured in Croatians are compared with ECSC/ERS reference values, some results of vital capacity and large respiratory airways may be assessed as pathological even though the subjects are objectively healthy, and some pathological results of flows through small respiratory airways may go unnoticed.

The limitations of our study were the age-range of our subjects and lack of anthropometric measurements. Due to the limited age range of our study population, our results are not applicable to men older than 64 and women older than 66. Considering that ventilatory functions vary with anthropologic characteristics, the measurements of anthropometric variables of Croatian population should be introduced into the research: sitting height, weight, hip/waist circumference and ratio, and body mass index. Such information could provide explanation for our findings, because the differences in fat free mass, chest dimensions, and the pressure generated by person's respiratory muscles might prove relevant.

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