Etude de l'application des équations de référence spirométriques Caucasiennes pour l'interprétation des données spirométriques d'une population Tunisienne adulte

Applicability of the Old European Respiratory Society/European Community for Steel and Coal Reference Equations For Spirometry Interpretation in Tunisian Adult Population

Mohamed Nour El Attar[1], Khaoula Hadj Mabrouk[1], Ahmed Ben Abdelaziz[2], Ahmed Abdelghani[3-4], Mohamed Bousarssar[3-5], Khélifa Limam[1-6], Chiraz Maatoug[1], Hmida Bouslah[1], Ameur Charrada[1], Sonia Rouatbi[7*8], Helmi Ben Saad[1-2-7-8]

1. Functional Exploration Laboratory. Occupational Medicine Group of Sousse. Tunisia.
2. Information Systems Management, Sahloul Medical Center, Sousse, Tunisia.
3. Research Unit: prevention secondaire après infarctus du mypcarde, N: 04/UR/08-18. Faculty of Medicine of Sousse. Sousse. Tunisia.
4. Pulmonary Department. Farhat HACHED Hospital. Sousse, Tunisia.
5. Medical Intensive Care Unit. Farhat HACHED Hospital. Sousse, Tunisia.
6. Laboratory of Biochemistry. Faculty of Medicine. University of Sousse. Tunisia.
7. Laboratory of Physiology. Faculty of Medicine. University of Sousse. Tunisia.
8. Department of Physiology and Functional Explorations. Farhat HACHED Hospital. Sousse, Tunisia

RÉSUMÉ

Prérequis : Les laboratoires Tunisiennes d'explorations fonctionnelles respiratoires acceptent, par défaut, les anciennes équations de référence spirométriques établies pour les Caucasians par la Société Respiratoire Européenne et par la Communauté Européenne du Charbon et de l'Acier alors que des normes spirométriques propres aux adultes Tunisiens sont disponibles.

Objectif : Comparer, selon les deux équations de référence, le profil spirométriques d'un échantillon d'adultes tunisiens.

Population et méthodes : Les données spirométriques de 1192 travailleurs adultes âgés de 18 à 60 ans ont été enregistrées. Les valeurs de référence et les limites inférieures de la normale (LIN) ont été calculées à l'aide des deux équations de référence. Les définitions spirométriques suivantes ont été retenues: Deficit Ventilatoire Obstructif (DVO) proximal: rapport entre le Volume Expiratoire Maximal à la première Seconde et la Capacité Vitale Forcéee (VEMS/CVF) < LIN. DVO distal: VEMS/CVF > LIN et CVF> LIN et débit expiratoire maximal médian < LIN. Tendance vers un Déficit Ventilatoire Restrictif (TDVR): VEMS et CVF < LIN. Le profil spirométrique de chaque sujet a été determiné selon les deux équations de référence.

Résultats : Selon les équations de référence Tunisiennes, 34%, 7%, 37% et 19% des resultats spirométriques ont été interprétés comme normaux et comme ayant un DVO proximal, un DVO distal et une TDVR, respectivement. Selon les équations de référence Caucasiennes, 85%, 3%, 9% et 2% des resultats spirométriques ont été interprétés comme normaux et comme ayant, un DVO proximal, un DVO distal et une TDVR, respectivement. En utilisant les équations de référence Caucasiennes, l'erreur de classification a été grande pour le DVO proximal, pour le DVO distal et pour la TDVR, respectivement, 68%, 94% et 89%.

Conclusion : Nos résultats montrent que l'utilisation des anciennes equations de référence spirométriques établies chez des Caucasians entraîne une mauvaise interprétation des données spirométriques dans une proportion importante d'adultes Tunisiens.

Mots-clés

Poumon, Spirométrie, Valeur Référence, Tunisie, Race Caucasienne, groupe Ethnique

SUMMARY

Background : Tunisian pulmonary functional laboratories accept the default settings for reference equations (European Respiratory Society/European Community for Steel and Coal (ERS/ECSC1983) offered by the manufacturer even though adult Tunisian reference equations (Tunisian1995) are available.

Objective : To compare the spirometric profile of Tunisian subjects, according to the two reference equations.

Population and methods : Spirometric data were recorded from 1192 consecutive spirometry procedures in adults aged 18-60 years. Reference values and lower limits of normality (LLN) were calculated using the two reference equations. Applied definitions: large airway obstructive ventilatory defect (LAOVD): ratio between the 1st second expiratory volume and forced vital capacity (FEV1/FVC) < LLN. Small AOVD (SAOVD): FEV1/FVC > LLN and FVC > LLN and maximal mid-expiratory flow < LLN. Tendency through a restrictive ventilatory defect (TRVD): FEV1 and FVC < LLN. The spirometric profile, according the two reference equations, was determined.

Results : Using Tunisian1995 reference equations, 34%, 7%, 37% and 19% of spirometry records were interpreted as normal, and as having, LAOVD, SAOVD and TRVD, respectively. Using ERS/ECSC1983 reference equations, 85%, 3%, 9% and 2% of spirometry records were interpreted as normal, and as having, LAOVD, SAOVD and TRVD, respectively. Using the ERS/ECSC1983 reference equations, misclassification was worse for LAOVD, for SAOVD and for TRVD, respectively, 68%, 94% and 89%.

Conclusion : Our results showed that the use of the old Caucasian reference equations resulted in misinterpretation of spirometry data in a significant proportion of subjects. This could result in inappropriate diagnosis and/or management.

Key-words

Lung, Spirometry, Reference Values, Tunisia, Caucasian Race,Ethnic Groups

Unlike the majority of biological indices in medicine, spirometry data varies with age [1-4], height [5, 6], sex and ethnicity [6-8]. Therefore, spirometry results need to be compared to reference equations (norms, predicted or reference values), and Lower Limit of Normal (LLN) and upper limit of normal that are appropriate for the individual being tested [9, 10]. The first step in diagnosing abnormality of spirometry in individuals is to define whether they are within or outside the healthy subject's normal range [below the LLN, normal or greater than the upper limit of normal] [2, 9, 11]. The second and more important step is to diagnose and evaluate the severity of the Obstructive Ventilatory Defect (OVD) or the Restrictive Ventilatory Defect (RVD) and airway obstruction reversibility if it is needed [10-13]. Usually, spirometric norms are obtained from reference equations derived from studies on "normal" or "healthy" people [1-9]. In addition, it is often recommended that pulmonary function laboratories should employ reference equations derived from subjects with similar characteristics (ethnic background, differences in body proportions, chest wall anatomy, mechanical properties of the thorax, parenchymal lung development, socioeconomic level and schooling level, parity, etc….) as the patients [11, 14]. The problem gets compounded when computerized equipments used for spirometry provide a numeric output of results derived from a limited (and often only a single) set of reference equations incorporated into the software. Often these reference equations are totally alien to the patient population being investigated. For example, the numeric output of results from spirometers built in Europe in 1983 (European Respiratory Society/European Community for Steel and Coal; ERS/ECSC1983) [4], which are commonly used in Tunisia and North Africa, is largely derived from Caucasian reference equations. Though it is perhaps best to use reference equations for patients from different ethnic backgrounds, it is usually not possible to do so because of the non-availability of spirometers with built-in local reference equations, and/or modification of existing software [2, 9, 11].

Many Tunisian pulmonary functional laboratories accept the default settings for reference equations for different age ranges offered by the manufacturer and are insufficiently aware of these problems. Tunisian clinicians and researchers, rely on the results obtained from ERS/ECSC1983 equations [4] incorporated into the software of spirometers, even though reference equations are available for several Tunisian populations (children [15], adults (Tunisian1995) [3] and older [5, 6] subjects).

The present study is designed to assess the impact of applying the old ERS/ECSC1983 spirometric reference equations [4] for the interpretation of results of routine spirometry performed in Tunisian adults' population.

POPULATION AND METHODS

Study design

We performed this cross-sectional study over a one-year period (February 2012- January 2013) in the Functional Exploration Laboratory at the Occupational Medicine Group of Sousse (altitude < 100 m), Tunisia. Approval for the study, from a hospital Ethics Committee wasn't needed, because the spirometry was done as a routine exam.

Study population

The target population consisted of a group of subjects aged 18 years old and more, working in Sousse. They were recruited from local workers visiting the Functional Exploration Laboratory at the Occupational Medicine Group of Sousse. The aforementioned offers several medical tests (electrocardiogram, visual test, audiogram and spirometry) as a routine service to local workers (subjects or patients). Approximately 3500 spirometry procedures are performed annually and workers are addressed by occupational physicians for several reasons: record review of employment, working in a risk position or dangerous workplace (i.e., dust, glue,...), further investigation of a complaint (i.e., dyspnea, cough, ...), control of a known respiratory illness and cigarettes or narghile smoking. Reasons for performing spirometry, as well as other clinical details, were not analyzed further. The following inclusion criteria were applied: age between 18 and 60 years; complete records and technically acceptable and reproducible spirometry maneuvers.

Collected data

The following medical and smoking data were collected: socioeconomic level, history of cigarettes or narghile smoking, main diseases and medications. The following anthropometric and spirometric data were collected, measured or calculated: age (year), sex (male/female), weight (kg), height (m) and Body Mass Index (BMI, kg.m-2), Forced Vital Capacity (FVC, l), 1st second Forced Expiratory Volume (FEV1, l), FEV1/FVC ratio (absolute value), Peak Expiratory Flow (l.s-1), Forced Expiratory Flow rate at the x% point of total volume to be exhaled (FEFX, l.s-1), Maximal Mid-Expiratory Flow (MMEF, l.s-1) and Forced Expiratory Time (s).

Data collection procedures

Medical data were collected using a simplified medical questionnaire composed of questions put to the subjects in local-Arabic dialect. Medical questions were about the following main diseases (heart, pulmonary, diabetes, anemia and rheumatologic) and current medications. Smoking habits were evaluated and data were collected relating to cigarette (packets-years) and narghile (narghiles-years) use [16-19].

The decimal age (accuracy to 0.10 years) was calculated from the date of measurement and the date of birth. Due to the failure of software to compute decimal age as the difference between test date and birth date, age was taken as the number of complete years from birth to the date of the study [20]. Standing height and weight were measured using a stadiometer and expressed to the nearest centimeter and kilogram, respectively. BMI (kg.m-2) was calculated.

Spirometry was carried out in the sitting position. To avoid the problem of variability due to different technicians and devices [2], all tests were performed between 9.00 am and 1.00 pm by only one qualified person. All subjects performed spirometry on a modern equipment [gold standard uni-directional digital volume transducer (Micro Medical Limited. PO Box 6, Rochester. Kent ME1 2AZ England)]. The Spida 5 software was used. The flow sensor of the spirometer was calibrated daily with a 3-liter syringe, to ensure performance. Spirometry was performed according to the international lung function testing guidelines [2]. A minimum of three reproducible FVC measurements were obtained [2]. FVC and FEV1 of the best two of the three selected measurements should not vary by more than 150 ml or 3%. The highest FVC and the highest FEV1 were computed, even if the two values did not come from the same curve [2].

Applied definitions and reference equations

Two socioeconomic levels were defined according to occupational status [21]: low (e.g. unskilled worker) and high (e.g. skilled worker, farmer, manager).

The subject was qualified as a lifelong non-smoker when the cigarette or narghile use were lower than five packets-years or lower than five narghiles-years, respectively, or when the sum of used cigarette and narghile was lower than five [16-19].

Depending on BMI, we distinguished between [22]: underweight (BMI < 18.5 kg.m-2), normal weight (18.5 kg.m-2   BMI < 25.0 kg.m-2), overweight (25.0 kg.m-2 BMI < 300.0 kg.m-2) and obesity (BMI   30.0 kg.m-2).

Reference values for spirometric data were generated using two reference equations: Tunisian1995 [3] and ERS/ECSC1983 [4].

Tunisian1995 reference equations [3], considered as the gold standard, were generated from spirometry studies performed on 977 healthy non smoking Tunisian adults, aged 18-70 years, using a plethysmograph (GOULD 2800 Autobox) and old spirometric recommendations’ were applied [4, 23, 24].

ERS/ECSC1983 [4] reference equations, routinely used at the Tunisian pulmonary function laboratories, were derived for Caucasian subjects aged 5-70 years from previously published reference equations [25]. In addition, in the North African population, it has been suggested by the ERS that reducing corresponding Caucasian values by 0.45 l and 0.40 l (respectively for males and females) and by 0.70 l and 0.60 l (respectively for males and females) might approximate predicted values for, respectively, FEV1 and FVC [4, 26].

Spirometric data were expressed in absolute values and as a percent of reference values (100 x measured value/reference value) according to Tunisian1995 (%Ref Tunisian1995) and to ERS/ECSC1983 (%Ref ERS/ECSC1983) reference equations [3, 4]. LLN were calculated using lower 95% confidence interval (95% CI) [9] derived from the regression equations being used. Any observed value lower than its corresponding LLN was considered abnormal [1]. Large Airway Obstructive Ventilatory Defect (LAOVD) was defined as a “FEV1/FVC ratio < LLN” [9]. Small Airway Obstructive Ventilatory Defect (SAOVD) was defined as the association of a “FEV1/FVC ratio   LLN” and a “FVC   LLN” with a “MMEF < LLN” [27]. Although a true Restrictive Ventilatory Defect (RVD) can be diagnosed only on demonstration of a reduced total lung capacity, a Tendency through RVD (TRVD) was inferred from spirometry results for categorical comparison purposes only. A record with “FEV1 < LLN” and “FVC < LLN” and “FEV1/FVC   LLN” was categorized as having a TRVD [9]. A Mixed Ventilatory Defect (MVD) was defined as the association of a “FEV1/FVC ratio <LLN” and a “FVC < LLN” and a “FEV1< LLN” [9].

Statistical analysis

Data distribution: the Kolmogorov-Smirnov test was used to analyse variables distribution [28]. When the distribution was normal and the variances were equal, the results were expressed by their means±SDs and 95% IC. If the distribution wasn’t normal, the results were expressed by their medians (1st-3rd quartiles).

Data comparison: the chi-2 test was used to compare percentages. A non parametric test (Wilcoxon matched pairs test) [28] was used to compare %Ref calculated from the two reference equations [3, 4].

Spirometry profiles: spirometry results (normal, LAOVD, SAOVD, TRVD, MVD) were interpreted for each subject. Spirometry results obtained using the two reference equations were compared after construction of contingency tables. Agreement between classification of spirometry results using the two reference equations were calculated using the Kappa estimate [29]. The proportion of subjects having different interpretations using the two reference equations was calculated for all combinations of prediction strategies as a measure of discordance. This group represented individuals whose interpretation changed if another scheme for calculating LLN was used in place of the gold standard Tunisian1995 equations [3].

To assess how closely the LLNs obtained by ERS/ECSC1983 reference equations [4] matched those obtained by the Tunisian1995 reference equations [3], we calculated the difference between values estimated by the Tunisian1995 and the Caucasian equations [1, 4].

In order to assess if the values determined by the two reference equations could be used interchangeably, we calculated the limits of agreement for each set of the two reference equations, by using the Bland and Altman method [30]. Limits of agreement were used for comparison, with individual difference (measured value minus LLN reference value for FEV1 or FVC) plotted against the corresponding mean value [30]. From these data, limits of agreement were then calculated [mean difference between measured and LLN (FEV1 or FVC) ± 1.96 SD].

Comparison after FVC and FEV1 values adjustment according to ERS: comparisons between FVC and FEV1 predicted from the two reference equations were also made after adjustment recommended by the ERS [26].

All mathematical computations and statistical procedures were performed using Statistica statistical software (Statistica Kernel version 6; Stat Software. France). Significance was set at the 0.05 level.

RESULTS

Descriptive data

Among the 3010 explored subjects, only 1192 (40%) were retained for analysis. The reasons of non-inclusion were the following: age < 18 years or > 60 years (n=128), incomplete records (n=291), technically inacceptable spirometry maneuvers (n=691) and non-reproducible spirometry maneuvers (n=708).

Figure 1 exposes the distribution of the total sample according to sex, age and height ranges. Fewer subjects aged < 25 years or   55 years were included, respectively, 5.9% and 5.4%. Fewer subjects (2.3%) having a height range of 1.43-1.55 cm were included.

Table 1 exposes the characteristics of the total sample. The last included a significantly higher percentage of males, of subjects with a low socioeconomic level and of smokers, respectively, 91.3%, 80.8% and 53.7%. Fewer subjects with obesity were included (18.8%).

Analytical data

Comparison of measured spirometric data expressed as a % Ref from the two reference equations

Figure 1 : Distribution of the total sample (n=1192) according to sex, age and height ranges. n: number. Numbers between brackets (=x/y) refer to the number of females (x) and males (y).

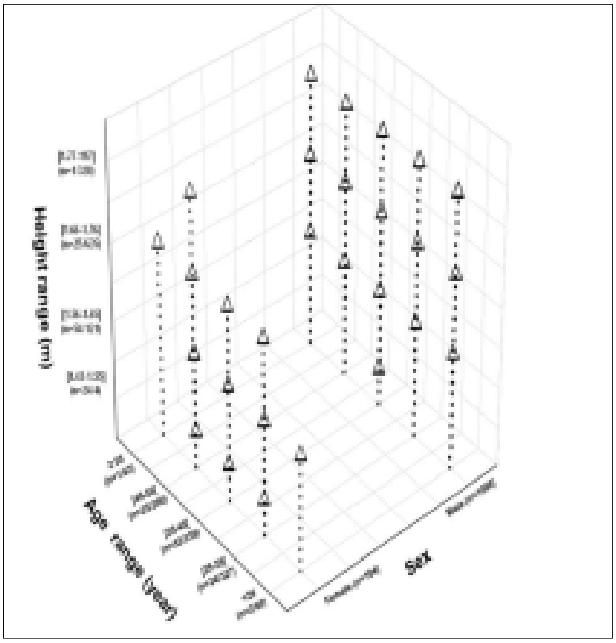

Table 1 : Descriptive data of the local workers visiting the functional exploration laboratory at the occupational medicine group of Sousse, Tunisia (n=1192).

Quantitative data (data are mean±SD (95% IC))		
Age *(year)*		39.57±8.51 (24.82-55.72)
Height *(m)*		1.72±0.07 (1.60-1.84)
Weight *(kg)*		78±14 (58-102)
Body mass index *(kg.m⁻²)*		26.3±4.2 (20.2-33.7)
Forced vital capacity (FVC, l)		4.38±0.80 (3.04-5.75)
1st second forced expiratory volume (FEV_1, l)		3.53±0.70 (2.34-4.70)
Maximal mid-expiratory flow *(l.s⁻¹)*		3.62±1.19 (1.95-5.67)
Peak Expiratory Flow *(l.s⁻¹)*		8.58±1.83 (5.57-11.64)
Forced expiratory flow rate at the 50% point of total volume to be exhaled (l.s⁻¹)		4.43±1.36 (2.20-6.63)
Forced expiratory flow rate at the 75% point of total volume to be exhaled (l.s⁻¹)		7.39±1.86 (4.32-10.48)
Quantitative data (data are median (1st-3rd quartiles))		
FEV_1/FVC (absolute value)		0.81 (0.77-0.85)
Forced expiratory flow rate at the 25% point of total volume to be exhaled (l.s⁻¹)		1.57 (1.17-2.01)
Forced expiratory time (s)		4.99 (4.19-5.95)
Qualitative data (data are numbers (%))		
Sex	*Female*	104 (8.7)
	Male	1088 (91.3)[a]
Socioeconomic level	*High*	197 (19.2)
	Low	824 (80.8)[a]
Obesity status	*Underweight*	15 (1.3)
	Normal weight	468 (39.3)
	Overweight	484 (40.6)
	Obesity	225 (18.8)[b]
Smoking status	*Smoker*	640 (53.7)
	Non-smoker	552 (46.3)[a]

Socioeconomic level was determined in only 86% of the subjects.
ap < 0.05 (chi-2): qualitative data for the data.
bp < 0.05 (chi-2): “underweight, normal weight and overweight” vs. “obesity”

All measured spirometric data expressed as %Ref ERS/ECSC1983 were significantly higher than those expressed as %Ref Tunisia1995 [mean±SD (95% IC) of FEV1, FVC, FEV1/FVC, MMEF and FEF75 were, respectively, 95±13 (94-95) vs. 85±12 (85-86), 101±12 (100-101) vs. 91±11 (90-92), 100±8 (100-101) vs. 98±8 (98-99), 89±26 (87-90) vs. 70±20 (69-71) and 96±22 (95-98) vs. 92±21 (91-93)].

Comparisons of the percentages of subjects with spirometric data lower than the LLN range according to the two reference equations

The percentages of Tunisian subjects having measured spirometric data lower than the LLN ranges were significantly lower with the ERS/ECSC1983 reference equations when compared with Tunisian1995 reference equations (respectively, 9% vs. 43% for FEV1, 2% vs. 22% for FVC, 4% vs. 10% for FEV1/FVC, 13% vs. 59% for MMEF and 7% vs. 17% for FEF75).

Table 2 exposes the mean bias and limits of agreement for LLN, for FVC and FEV1 on comparison of ERS/ECSC1983 reference equations with Tunisian1995 reference equations. The conclusion of this table was that the ERS/ECSC1983 reference equations consistently over-predicted LLN for FVC and FEV1 for males, females and the total sample.

Table 2 : Mean differences' and limits of agreement for the lower limit of normal for forced vital capacity (FVC) and 1st second forced expiratory volume (FEV1) on comparison of Caucasian with Tunisian1995 reference equations.

Males		Females		Total sample	
FVC (l)	FEV1 (l)	FVC (l)	FEV1 (l)	FVC (l)	FEV_1 (l)

Comparison of spirometry interpretation by ERS/ECSC1983 and Tunisian1995 reference equations

Table 3 : Comparison of spirometry interpretation by Caucasian and Tunisian1995 reference equations

		Tunisian1995				
		Normal (n=411)	LAOVD (n=80)	SAOVD (n=439)	TRVD (n=227)	MVD (n=35)
ERS/ECSC1983	Normal (n=1015)	411 (100.00)	17 (21.25)	414 (94.31)	170 (74.89)	3 (8.57)
	LAOVD (n=38)	0 (0.00)	26 (32.50)	0 (0.00)	2 (0.88)	10 (28.57)
	SAOVD (n=104)	0 (0.00)	37 (46.25)	25 (5.69)	29 (12.78)	13 (37.14)
	TRVD (n=28)	0 (0.00)	0 (0.00)	0 (0.00)	26 (11.45)	2 (5.71)
	MVD (n=7)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	7 (20.00)

LAOVD: Large Airway Obstructive Ventilatory Defect. SAOVD: Small Airway Obstructive Ventilatory Defect. TRVD: Tendency Through Restrictive Ventilatory Defect. MVD: Mixed Ventilatory Defect.
Data are number (%) of subjects.
Percentage is calculated as following: number of subjects/total of subjects for each spirometry interpretation.

Table 3 exposes the comparison of spirometry interpretation by ERS/ECSC1983 and Tunisian1995 reference equations. The main conclusions of this table were:

I) Using Tunisian1995 reference equations, 80 (6.71%), 439 (36.83%), 227 (19.04%) and 35 (2.94%) spirometry records were interpreted as having, LAOVD, SAOVD, TRVD and MVD, respectively.

II) Using ERS/ECSC1983 reference equations, 38 (3.18%), 104 (8.72%), 28 (2.35%) and 7 (0.59%) spirometry records were interpreted as having, LAOVD, SAOVD, TRVD and MVD, respectively.

III) Among the 411 normal records according Tunisian1995 reference equations, no one was classified as being abnormal using the ERS/ECSC1983 reference equations.

IV) Using the ERS/ECSC1983 reference equations, misclassification was worse for LAOVD, for SAOVD, for TRVD, and for MVD, respectively, 67.50%, 94.31%, 88.55% and 80.00%. The ERS/ECSC1983 reference equations misclassified results in 58.47% subjects.

Table 4 exposes the Kappa estimate of agreement, and percentage of misclassified results, for spirometry interpretation between Tunisian1995 and ERS/ECSC1983 reference equations. The last demonstrated poor agreement (in females, males and total sample) with high misclassification rates (eg. 58.47% for the total sample).

Comparison after FVC and FEV1 values adjustment

Table 4 : Kappa estimate of agreement, and percentage of misclassified results, for spirometry interpretation between Tunisian1995 and Caucasian reference equations.

Males	Females	Total sample
Kappa estimate of agreement (95% confidence limits)		
0.144 (0.090 to 0.137)[a]	0.298 (0.173 to 0.410)[a]	0.124 (0.100 to 0.147)[a]
Percentage of misclassified results		
61.12	30.76	58.47

[a] $p < 0.05$ (Kappa estimate).

Measured and adjusted FEV1 and FVC expressed as %Ref ERS/ECSC1983 were significantly higher than these expressed as a %Ref Tunisian1995 reference equations (respectively, 108±15% vs. 85±12% and 120±15% vs. 91±11%). In addition, the percentages of Tunisian subjects having a measured FEV1 and FVC lower than the LLN ranges are significantly lower with the ERS/ECSC1983 reference equations when compared with Tunisian1995 reference equations (respectively, 2.0% vs. 43.0% and 0.3% vs. 22.0%).

DISCUSSION

The main result of the present study conducted on 1192 workers was that the use of the older Caucasian ERS/ECSC1983 reference equations leads to misinterpretation of spirometry data in a significant proportion of adult's Tunisian subjects. This could result in inappropriate diagnosis and/or management.

Methodology discussion

Study design: one of the positive points of the present study is its prospective design. Some caution should be warranted when interpreting the results of cross-sectional studies in volunteers because of a possible selection bias and cohort effects [31]. Thus, longitudinal studies analysed by appropriate statistical models are necessary to properly choose the more adapted reference equations [9]. Although, no statistical methods have been used to choose subjects or to calculate their number, the fact that many private or government-owned firms in different areas of Sousse, Tunisia were included gives a reasonable degree of confidence in the data. The large number (n=1192) of spirometry records included for analysis ensured adequate representation of all categories of age and height (Figure 1) allowing confident identification of even small differences without any bias. One limit of our study is the fewer number of females (8.7% of the total sample, table 1). In fact, the percentage of Tunisian active females is low at almost 25% [32].

Population source: the subjects studied herein represent a population that undergoes routine pulmonary function testing at our Functional Exploration Laboratory. The relatively higher proportion (34.5%, table 3) of normal spirometric records in this study is explained by the fact that they were included as a record review of employment. Our recruitment mode was similar to that of the retrospective Indian study [33]. The last, designed to assess the impact of applying commonly used Caucasian reference equations [4, 34-36] for the interpretation of results of routine spirometry performed in Indian patients, has been done for over 4 years. Spirometry was offered as a routine service to both outpatients and inpatients [33]. As recommended [1, 33], though the results from this study can only be strictly applied to a similar population (Arab, Mediterranean or North African populations) tested with similar instruments and procedures, the conclusions can perhaps be generalized to other situations, as well, with minor differences.

Applied inclusion and non-inclusion criteria: almost 60% of the subjects addressed for spirometry, during the year 2012, weren't included. In a study of adults carried out in a laboratory [37] that adhered to the quality assurance program, >30% of measurements were discarded because they did not meet American thoracic society quality criteria [38]. The two main non-inclusion criteria were technically inacceptable and/or non-reproducible spirometry maneuvers. These two criteria, not applied in the Indian study [33], are two noticeable points for our study. In fact, the obtained spirometric results depend on technical methods. The percentage of subjects excluded, because of incomplete records was higher than those of the Indian study [33] (respectively, 10% vs. 1%).

Spirometry measurements and definition: we have applied the 2005 international guidelines for spirometry [2, 9, 11]. As in another study [33, 39] having the same aim as our's, we applied the international definitions based on 95% IC [9]. When interpreting the spirometry data, we compared the measured values with the reference values established in a "normal" population and thus standardized according to factors determining lung size [40]. Values outside the 95% IC were considered to be "abnormal" [40, 41].

Statistical analysis: the same statistical type of analysis applied in other studies [33, 39] having the same aims as our's were applied.

Results discussion

The accuracy with which lung function tests are interpreted hinges on the appropriateness of the selected reference dataset [9, 42]. Errors in interpretation, with respect both to overestimation and underestimation of lung function abnormalities, can occur if inappropriate reference equations are used [9, 42].

Tunisian clinicians and researchers, rely on the results obtained from ERS/ECSC1983 reference equations [4] incorporated into the software of spirometers, even though reference equations are available for several Tunisian populations [3, 5, 6, 15].

Can the Caucasian reference equations be used interchangeably with the Tunisian reference equations?

Our results, even adjusted according to ERS [26], revealed large difference and wide confidence limits between Caucasian [4] and Tunisian spirometric reference equations, therefore indicating that the two cannot be used interchangeably. What are the origins of differences?

Differences in pulmonary function among various racial and ethnic groups are well-known; and differences in body proportions, chest wall anatomy, mechanical properties of the thorax, and parenchymal lung development have been postulated as contributory factors [1-3, 34]. The ERS/ECSC1983 reference equations [4] imperfections are:

I) The onset age of lung function data decline with age is assumed a priori as the same for all lung function data and equal to 25 years;
II) Simple linear equations describing lung function data dependences on age higher than 25 years can reflect nonlinearity of these dependences inaccurately;
III) LLNs are determined as equations for means minus 1.645 x SD of differences between observed and reference values of lung function data;
IV) The equations are old, i.e. they have been prepared for previous generations and old procedures of examinations.

It has been generally suggested that lung volumes in North African subjects are smaller than corresponding values in Caucasians [4, 26]. Though such 'ethnic discounting', whose origin isn't clear, has been widely recommended, there is no firm evidence that it provides accurate estimates [43, 44].

Data on the utility of Caucasian reference equations in interpreting spirometry results in patients of other populations are sparse [33, 45, 46]. In a small study on 442 Spanish patients at a New Mexico hospital, local Hispanic reference equations were compared to three Caucasian reference equations in categorizing FVC and FEV1 as normal or abnormal [45]. In this report, 2-10% results were misclassified, depending on the reference equations used. In a large study on 14733 consecutive spirometry procedures in Indian adults, results showed that the use of Caucasian prediction equations, or a fixed percentage of their reference values, resulted in misinterpretation of spirometry data in a significant proportion of patients [33]. In a study done on 2745 adults, the main conclusion was that ERS/ECSC1983 cannot be applied in Poland [46].

What is the impact of applying commonly used Caucasian reference equations for the interpretation of results of routine spirometry performed in the Tunisian adult population?

Our results highlighted some important facts about using Caucasian reference equations [4] in other populations, such as Mediterranean, North African or Arab populations. It is quite evident that these reference equations led to misinterpretation of spirometry data in a significant proportion of subjects or patients and which could result in inappropriate diagnosis and/or management. For example when using the ERS/ECSC1983 [4] reference equations, misclassification was worse for LAOVD (67.50%, table 3). The adjustment, according to ERS/ECSC1983 [26], of FVC and FEV1 values, worsened the problem of interpretation. For example, measured FEV1 expressed as percentage of ERS/ECSC1983 reference values [26], before and after adjustment [4], were respectively 95±13% and 108±15%. An important aspect brought out by our analysis was that reference Tunisian1995 FEV1 values were much lower than Caucasian values [26]. Based solely on this observation, we would not recommend a reduction in reference values for both these lung volumes for approximation from Caucasian reference equations [4, 26].

We also attempted to quantify agreement between reference values of different spirometric parameters using Tunisian1995 and the Caucasian equations [3, 4]. This approach had definite advantages over merely reporting correlation or regression coefficients, as it provided a numerical estimate of how similar are values obtained from two distributions, and whether results from the two approaches could be used interchangeably [30]. We observed wide variations in the mean bias for all spirometric parameters studied (Table 2). We also calculated the limits of agreement, which represented a numerical expression of range in which 95% of the bias values were likely to be situated (Table 4). Our findings suggested a rather poor agreement between Caucasian and Tunisian1995 reference equations [3, 4].

CONCLUSION

In conclusion, the results of the current study don't support the use of the Old Caucasian reference equations to interpret clinical and research results in contemporary Tunisian subjects.

PERSPECTIVE

Recently, the ERS/Global lung initiative task force released Multi-ethnic reference values for spirometry spanning 26 countries including Tunisia and Algeria [1]. These global all-age equations, encouraged by users and multiple international respiratory societies, are now implemented by manufacturers of spirometric devices and will be very soon commercialized in North Africa. Multi-ethnic reference values [1] may not be suitable for use in Tunisian adults' population and as recommended [1], more studies are required in Arab population. It is necessary and urgent to ascertain, in a healthy group, how well the recent Multi-ethnic reference values fit contemporary Tunisian spirometric data.

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