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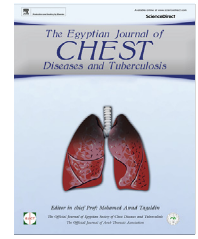

ORIGINAL ARTICLE

Spirometric "Lung Age" estimation for North African population

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KEYWORDS

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Abstract *Background:* Published reference equations predicting Estimated-Lung-Age (ELA) did not reliably predict Chronological-Lung-Age (CLA) data in North African population.

Aims: To develop and to validate novel reference equations for ELA from varied anthropometric data and FEV_1.

Methods: Applying multiple regression analysis, equations predicting ELA were invented using data from 540 never-smokers with normal spirometry (*group I*). Validation was made based on data from 41 never-smokers with normal spirometry (*group II*). Equations were further applied for 91 subjects with confirmed COPD.

Abbreviations: BMI, Body-Mass-Index; BSA, Body-Surface-Area; CLA, Chronological-Lung-Age; COPD, Chronic Obstructive Pulmonary Disease; deltaLA, CLA minus ELA; ELA, Estimated-Lung-Age; FEF_x, Forced Expiratory Flow when x% of FVC has been exhaled; FEV_1, first second Forced Expiratory Volume; FVC, Forced Vital Capacity; LA, Lung-Age; LOA, Limits-Of-Agreement; LLN, Lower-Limit-of-Normal; MMEF, Maximal Mid-Expiratory Flow; *n*, number; OSA, Obstructive Sleep Apnea; PEF, Peak Expiratory Flow; RSD, Residual Standard Deviation; SD, Standard-Deviation; ULN, Upper-Limit-Of-Normal; *r*, coefficient of correlation; r^2, coefficient of determination; 95% CI, 95% confidence interval.

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Results: Novel regression equations allowing prediction of reference value of ELA and normal limits of difference between ELA and CLA were elaborated in both sexes. In males, ELA (yrs) = 42.85 − 20.74 × FEV_1 (L) + 47.41 × Body Surface Area (m^2) − 0.62 × Body-Mass-Index (BMI, kg/m^2). In females, ELA (yrs) = 64.64 − 8.00 × FEV_1 (L) − 0.17 × BMI (kg/m^2) + 8.82 × Height (m). Normal limits of difference between ELA and CLA were ±16.9 yrs in males and ±14.8 yrs in females. Established equations predicted ELA of *group II* with no significant difference between CLA and ELA in either sex (respectively, 42.9 ± 16.6 vs. 40.3 ± 13.7 yrs in males, 42.0 ± 13.5 vs. 45.6 ± 7.7 yrs in females) ELA was significantly older than CLA age only in COPD with grades III and IV ((ELA minus CLA) (yrs) averaged, respectively, +21.7, +26.4).

Conclusion: North African reference equations enrich the World Bank of reference equations from which the physician should choose according to the patient's ethnic background.

Introduction

The single most useful intervention to improve lung function in smokers, with or without, Chronic Obstructive Pulmonary Disease (COPD) is smoking cessation [1,2]. One way to increase the quit rate in smokers could be to communicate lung function results in a manner that is easily understood and stimulates the desire to quit [1].

To conquer the difficulty existing in the raw results of spirometric measurements, the concept of Estimated-Lung-Age (ELA) has been proposed [3]. ELA is an estimate that uses the observed spirometric variable (often FEV_1 for first second Forced Expiratory Volume) of a smoker to calculate the approximate age of a healthy non-smoker with the same spirometric variable based on reference values [3]. Its basis of interpretation relies upon comparison of the Chronological-Lung-Age (CLA) values with ELA predicted from available reference equations [3–6]. Morris and Temple [3] proposed the concept of ELA about 28 years ago, for USA population using earlier American spirometry reference equations [7]. Four models of ELA reference equations were developed and the most relevant model to determine ELA values was the one using FEV_1 [3].

To extend the clinical application of Lung-Age (LA), three other reference equations predicting ELA have been recently published [4–6]. In 2010, two reference equations were developed by Newbury et al. and by Hansen et al. for, respectively, South Australian and USA populations [4,5]. In 2012, Yamaguchi et al. [6] have developed novel regression equations for Japanese population. Hansen et al. [5] proposed a simplified equation allowing LA estimation from the ratio between FEV_1 and Forced Vital Capacity (FVC). Newbury et al. [4] applied the same methods described by Morris and Temple [3] with the equations being solved for age. Yamaguchi et al. [6] have presented equations including various spirometric parameters such as FVC, FEV_1, FEV_1/FVC ratio, Peak Expiratory Flow (PEF), Forced Expiratory Flow when x% of FVC has been exhaled (FEF_x, FEF_{50} and FEF_{25}) and Maximal Mid-Expiratory Flow (MMEF). Only two authors [3,6] have proposed algorithms for judging the abnormality from spirometry ELA with presentation of a recommended sequence to interpret ELA [3] or a recommendation to use the Upper-Limit-of-Normal and Lower-Limit-of-Normal (ULN, LLN, respectively) [6], as recommended for spirometry [8]. These four published studies [3–6] presented several limitations, previously described [9]: low sample size [4], sample may not be representative of a normal population [3,4], skewed age distribution [3], use of old spirometric data or equipment [3,5], application of old spirometric methods [4], mathematical and statistical flaws [3–5], wide variation in ELA [4]. These methodological shortcomings explain some discrepancies in the findings [9]. In North African population, it was strongly suggested that existing LA equations [3–6] are in need of review [9]: these reference equations did not reliably predict CLA data in a large group of Tunisian healthy adults. In addition, among the four published equations [3–6], it was recommended to use, those developed for healthy Japanese subjects aged 25–87 years [6]. The recommendation was justified by several reasons [9].

How to evaluate "spirometric" ELA and what method is approvable? This question was asked in 2011 [10], in order to promote the development of ethnic-specific ELA regression equations in various races. The need for normal values specific to North African populations has been demonstrated for several physiological parameters [9,11–18]. So, the applicability and the reliability of published ELA reference equations [3–6] should be assessed with regard to North African adult's population, in order to avoid erroneous clinical interpretation of ELA data in this population.

Based on these backgrounds, the aims of the present study are

(i) To establish novel regression equations allowing prediction of the reference value of ELA and its normal limits using the data harvested from a large number of healthy Tunisian never-smokers with normal spirometric measurements; and to propose an algorithm for judging the abnormality of the ELA.
(ii) To validate the developed equations using the data obtained from a second group of healthy never-smokers with normal spirometry and two groups of subjects with deteriorating pulmonary function; and
(iii) To compare the novel North African ELA reference equations with those of Yamaguchi et al. [6].

Population and methods

Study design

A large part of the design and methods was previously described [9].