Respiratory Medicine 124 (2017) 44–48

Contents lists available at ScienceDirect

Respiratory Medicine

journal homepage: www.elsevier.com/locate/rmed

Longer duration of asthma is significantly associated with increased RV/TLC ratio

Anupama Tiwari [a, d], Kazi Rahman [c], Belayneh Abejie [b], Vipul V. Jain [a], Jose Joseph Vempilly [a, *]

[a] Division of Pulmonary/Critical Care, UCSF-Fresno, USA
[b] Division of Occupational Medicine, UCSF-Fresno, USA
[c] Department of General Internal Medicine, UCSF-Fresno, USA
[d] East Carolina University, Greenville, NC, USA

ARTICLE INFO

Article history:
Received 18 March 2016
Received in revised form
19 December 2016
Accepted 31 January 2017
Available online 2 February 2017

Keywords:
Duration of asthma
RV/TLC ratio
FEV1/FVC ratio
General linear model

ABSTRACT

Background: Although FEV1/FVC ratio has been shown to be negatively associated with longer duration of asthma; an association between RV/TLC ratio and longer duration of asthma has not been explored.
Material and methods: Patients with established asthma for more than a year and met inclusion and exclusion criteria were recruited. Data obtained by questionnaire after informed consent was obtained, Pulmonary function tests and laboratory results were collected through chart review. Correlation and multiple linear regressions were used to analyze the data.
Results: Among the 93 subjects, 61 were women. The mean age of patients was 58 ± 15 years, and the mean duration of asthma was 21 ± 18 years. The ethnic composition included: Caucasians 64%, Hispanics 28% and other groups 8%. The FEV1/FVC ratio was not significantly associated with duration of asthma ($R2 = 0.15$, $p = 0.05$). However, the RV/TLC ratio was significantly associated with duration of asthma ($R2 = 0.46$, $p < 0.001$).
Conclusion: RV/TLC ratio may be a better indicator than FEV1/FVC ratio to detect airway obstruction related to longer duration of asthma. Lung volume measurements should be done in addition to spirometry to detect changes related to airway obstruction in patients with longer duration of asthma.

1. Introduction

Asthma is a clinical syndrome characterized by intermittent or persistent dyspnea, cough and wheeze. Nevertheless, the clinical features of asthma and COPD can overlap making it difficult to differentiate the two syndromes [1] Asthma symptoms have been attributed to airflow obstruction resulting from airway inflammation [2]. Presence of obstruction has been diagnosed by the disproportionate decrease of FEV1 (forced expiratory volume in 1 s) over FVC (forced vital capacity) leading to a low FEV1/FVC ratio. However, there has been considerable debate regarding the use of fixed value versus the lower limit of FEV1/FVC ratio to diagnose obstruction in asthma [3,4]. Although a trend for decline in FEV1% predicted value with time has been observed in children with persistent asthma symptoms [5], previous studies have shown that spirometry indices do not correlate with symptoms or severity of asthma [6,7]. However, Sorkness and associates observed an association between abnormal lung volumes and severe asthma [8]. A recent study with simultaneously measured lung volumes and spirometry in subjects with asthma showed that there were significantly more frequency of abnormal residual volume (RV) and RV/TLC ratio (residual volume/Total lung capacity) than the frequency of abnormal FEV1/FVC ratios, percent predicted FEV1 values or the FEV1 reversibility [9,10]. These findings are consistent with previous observation that spirometric criteria may be used to guide, but not to diagnose airflow obstruction in subjects with asthma [9]. A cross sectional study of non-smoking subjects with asthma over the age of sixty, showed a significant association between increased FRC in subjects with longer duration of asthma [11]. However, this study did not utilize RV/TLC ratio to define obstruction or to explore relationship with the duration of asthma.

* Corresponding author. Division of Pulmonary & Critical Care Medicine, Department of Internal Medicine, UCSF Fresno, 155 N Fresno St., Fresno, CA 93701, USA.
E-mail address: jjoseph@fresno.ucsf.edu (J.J. Vempilly).

http://dx.doi.org/10.1016/j.rmed.2017.01.011
0954-6111/

Therefore, we explored the relationship between RV/TLC ratio and duration of asthma and enumerate the proportion of subjects with abnormal spirometric and lung volume abnormalities in this non-age restricted cross-sectional study.

2. Methods

Study subjects: All patients with an established diagnosis of asthma and with persistent asthma symptoms for the last 12 months that fulfilled the inclusion and exclusion criteria were enrolled. All subjects were recruited from a university clinic between June 2012 and May 2014. The inclusion criteria were: presence of persistent asthma symptoms, use of asthma control medications for more than a year, and having had a lung function test within 11 months from the date of interview. The exclusion criteria were: subjects with a diagnosis of COPD based on lung function study, subjects with DLCO <70% of predicted normal, subjects with chronic respiratory symptoms due to pulmonary fibrosis, sarcoidosis, extrinsic allergic alveolitis and congestive heart failure, and subjects not willing to sign an informed consent for the study. The protocol and conduct of this study was approved by the local IRB.

Data Collection: After obtaining an informed consent, asthma questionnaire was administered by trained physicians during clinic visit and or by direct telephone interview. The questionnaire consisted of information regarding patient demographics, duration of asthma and symptoms severity as suggested in National Asthma guidelines.[2] Patient charts were reviewed for additional information including for most recent pulmonary function tests (PFT). All lung function tests were done as per ATS/ERS recommendations [12,13]. The lung volume measurement were done using body plethysmography by Medical Graphics Corporation, St. Paul, Minnesota – UåSA. Abnormal test values were defined by criteria previously published [9].

Data Analysis: Gender ethnicity and tobacco use were treated as independent nominal variables. Similarly, age, height, weight, and duration of asthma were used as continuous co-variables. Bivariate correlations between duration of asthma, FEV1/FVC, RV/TLC, age, height, and weight were done. Following this, a general linear model regression analysis was conducted using FEV1/FVC ratio and RV/TLC as outcome variables. Predictor variable with significant Co-linearity were excluded from the model. The relationship between FEV1% predicted value and FEV1/FVC ratio, total lung capacity and RV were plotted using locally weighted scatter plot curves (LOWESS) to explore the pattern of variation of later variables with FEV1% decline. SPSS version 23 was used for the analysis. A 2 sided p value < 0.05 was considered statistically significant.

3. Results

Table 1 shows the baseline characteristics of study subjects. The mean age of ninety-three patients was 58 ± 15 years, and the mean duration of asthma was 21 ± 18 years. The mean Ethnic composition included: 64% Caucasians, 28% Hispanics and 8% others. While 66% were female subjects, smokers were 31% with a mean pack year of 7.6 ± 18 years. The clinical severity of asthma was mild persistent in 15%, moderate persistent in 45% and severe persistent in 40%. Fig. 1 shows the prevalence of abnormal lung function test results in study subjects. Fig. 2-A shows the linear relationship between actual values of FEV1 and FVC. There was a proportional decrease in FEV1 for every unit decrease in FVC value (r = 0.9) indicating the two variables were highly correlated. Fig. 2-B shows the trend lines using LOWESS for percent predicted values for FVC, TLC and RV plotted against FEV1% predicted values. The trend lines showed that FVC and FEV1 decline were proportionate while the RV increased disproportionately compared to TLC predicted values. Fig. 3A and 3B three shows the linear relationship between the duration of asthma to FEV1/FVC ratio and RV/TLC ratio. While there was significant linear correlation between the RV/TLC ratio and the duration of asthma (R-0.38, p < 0.001), there was no significant correlation between the duration of asthma and the FEV1/FVC ratio (R = 0.15, p = 0.13). Table 2 shows the results of general linear model analysis for outcome variable FEV1/FVC ratio against significant predictor variables. The model for FEV1/FVC ratio was of borderline significance (R^2 = 0.15, p = 0.05). However, the model for the outcome variable RV/TLC ratio (Table 3) was significant (R^2 = 0.46, p < 0.001). The independent correlation coefficient for RV/TLC ratio were: age β = 0.27 (0.18–0.37), duration of asthma β = 0.14 (0.06–0.22) and being a non-smoker β = -3.7 (−6.7 to −0.7).

Table 1
Demographics and laboratory values in study subjects.

Variable	Mean	Standard Deviation
Age	58	15
Height (centimeter)	166	11
Weight (pounds)	192	56
Duration of Asthma (Years)	21	18
FVC Actual	3.16 (86%)	0.94
FEV1 Actual	2.34 (82%)	0.72
FEV1/FVC Ratio	74	10
RV Actual	2.31 (119%)	0.68
TLC Actual	5.43 (98%)	1.28
RV/TLC Ratio	42.70	8.47
Diffusion Capacity % Predicted	85%	12.1
Serum total IgE (IU unit)	351	718
Eosinophil % of total count	4	4

Parenthesis shows % predicted values.

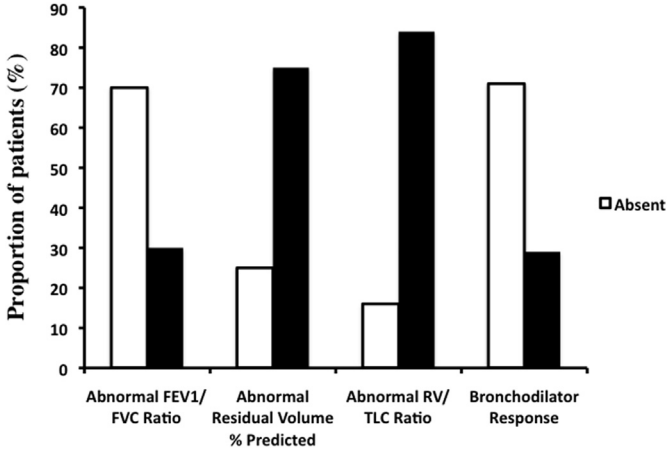

Fig. 1. Proportion of abnormal spirometry and lung volume indices in study subjects.

4. Discussion

Asthma has been characterized as a chronic inflammatory disease affecting large and small airways leading to airflow limitation [14–16]. Although FEV1/FVC ratio has been considered the gold standard to diagnose airflow obstruction, this ratio has not been shown to correlate with severity or symptoms of asthma [6,7]. Nevertheless, Cassino et al. observed a modest correlation between the duration of asthma and FEV1/FVC ratio in a group of age-restricted patients with asthma [11]. Although we observed a trend for an association between FEV1/FVC ratio and the duration of asthma, this finding was not statistically significant. In this