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ORIGINAL ARTICLE

Pulmonology

Can Plethysmography Identify Earlier Lung Function Changes in Asthmatic Children?

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Abstract

Background: Although in recent years, it has been noted that spirometry provides little information about lung function in children with asthma, as spirometry is normal in most cases, international guidelines still recommend spirometry for diagnosing and monitoring children with asthma. Spirometry measures dynamic lung volumes, while plethysmography measures static lung volumes. The aim of this study was to evaluate the role of plethysmography in identifying functional phenotypes in children with asthma.

Methods and Results: This observational study included 93 patients (boys [66.7%] and girls [33.3%], mean age of 8.6±3.1years) diagnosed with bronchial asthma (GINA, 2020). All patients were classified according to asthma severity. All patients underwent spirometry and plethysmography measurements. The reference values of functional parameters were based on Zapletal data. Air trapping was detected in 78.5% of patients according to residual volume (RV) data, 77.4% of patients according to RV/total lung capacity [TLC] data, 58% of patients according to functional reserve capacity [FRC]/TLC data, and 57% according to FRC data. Only 26.9% of patients, according to TLC, had distension (hyperinflation). 12.3% of the patients had the so-called pseudo-restriction phenotype or small airway obstruction syndrome, which involves increased RV, decreased FVC, and normal TLC.

There was no statistically significant relationship between RV and FEV_1 (r=-0.104, *P*=0.325). A weak negative correlation (r=-0.319, *P*<0.05) was found between RV/TLC and FVC. A weak negative correlation was determined between RV and age (r=-0.252, *P*=0.046). At the same time, we found a moderate positive correlation between TLC and RV/TLC (r=0.65, *P*<0.001). We studied the sensitivity and specificity of lung function variables (FEV_1, FVC, $FEF_{50\%}$, and specific airway resistance [sRaw]) to predict the presence of air trapping (RV>140%pred) and found none of these variables can discriminate the presence of air trapping.

Conclusion: Air trapping is the most common and earliest functional phenotype; thus, it is the most sensitive functional parameter for identifying functional abnormalities in asthma. It is present in all degrees of asthma severity. Spirometric variables cannot detect small-airway obstruction syndrome (air trapping); therefore, a plethysmographic measurement of pulmonary volumes is necessary. Functional physiological phenotypes such as air trapping, restriction, and pseudo-restriction are present in children with asthma and can only be identified by measuring lung volumes.**(International Journal of Biomedicine. 2024;14(4):569-574.)**

Kyewords: asthma • children • plethysmography • air trapping

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Abbreviations

FRC, functional reserve capacity; **FEV_1**, forced expiratory volume in 1 second; **$FEF_{50\%}$**, forced expiratory flow at 50% of FVC; **FVC**, forced vital capacity; **RV**, residual volume; **sRaw**, specific airway resistance; **TLC**, total lung capacity.

Introduction

From a functional point of view, asthma is characterized by the variable bronchial obstruction, reversibility, and bronchial hyperreactivity. Proximal and distal airways are involved in asthma, but the ability of spirometry to estimate the airways remains debatable.[1,2,3]

Except for expiratory flow, different anomalies of static lung volumes, such as air trapping,[4] restriction,[5] and pseudo-restriction,[1,6,7] are mentioned in asthma. An abnormal increase in lung volumes causes air trapping, usually at the expense of dynamic lung volumes such as inspiratory capacity and vital capacity. Several parameters are proposed as indicators of air trapping: functional reserve capacity (FRC), residual volume (RV), and RV/total lung capacity (TLC). Small airways are the primary site of physiologic obstruction in asthma,[8,9] and this dysfunction is seen in moderate-severe asthma,[10,11] mild asthma,[12,13] and asymptomatic patients.[14,15] Lung volume anomalies should prompt us to measure them, but asthma guidelines do not recommend this yet. Spirometry is still the internationally recommended measure[16-18] for asthma diagnosis and follow-up.

The question is: can plethysmography identify early functional changes in asthma, and is it necessary to search regularly for lung volume anomalies if spirometry can predict their existence?

As previously studied by Mahut et al.,[1] we tested the following hypotheses: 1. Since spirometry is normal in most children with asthma,[19-22] static lung volume measurement provides important data on lung function. 2. If air trapping is the most frequent functional phenotype, spirometric parameters cannot predict its existence.

The aim of this study was to evaluate the role of plethysmography in identifying functional phenotypes in children with asthma.

Materials and Methods

This observational study included 93 patients (boys [66.7%] and girls [33.3%], mean age of 8.6±3.1years) diagnosed with bronchial asthma (GINA, 2020), clinically stable for the past four weeks, without asthma exacerbation during the previous month. Exacerbation was considered to be the result of one or more of the following phenomena: hospitalization, use of parenteral prednisone for asthma, out-of-plan emergency visits, or specialist visits. Patients should be asymptomatic during the visit, clinically stable and without auscultatory changes, and cooperate to perform the spirometry. All patients were classified according to asthma severity.[16] Patients were told not to use short-acting beta-agonists for the last 6 hours and long-acting beta-agonists for the last 12 hours.

Equipment

All patients underwent spirometry and plethysmography measurements. The static lung volumes were measured with a constant-volume plethysmograph (MasterScreen Body Plethysmograph 4.3, Erich Jaeger GmbH, Würzburg, Germany),[23,24] and the dynamic lung volumes were measured with a spirometry test using a screen pneumotachograph (Screenmate; Erich Jaeger GmbH & Co., Höchberg, Germany). Lung volumes were measured according to ATS/ERS-2005 recommendations. Three acceptable maneuvers were performed to measure the expiratory flows. The end-of-test criteria were considered those set by the ATS/ERS task force.[24] The reference values of functional parameters were based on Zapletal data.[25] Parameters are expressed in percent predicted (pred).

Cutoffs for plethysmographic parameters of hyperinflation: FRC>120%pred, TLC>125%pred, RV>140%pred, RV/TLC>120%pred. Cutoffs for obstruction of spirometric variables: FEV1<80%pred, FEV1/FVC<90%pred, FVC<80%pred, FEF25%-75%<70%pred.

Statistical analysis was performed using the statistical software package SPSS version 20.0 (SPSS Inc, Armonk, NY: IBM Corp). Baseline characteristics were summarized as frequencies and percentages for categorical variables and mean (M) ± standard deviation (SD) for continuous variables. Pearson's correlation coefficient (r) was used to determine the strength of the relationship between the two continuous variables. Spearman's rank correlation coefficient (rs) was also used. Group comparisons concerning categorical variables were performed using chi-square or Fisher's exact tests. Sensitivity, Specificity, and Predictive Values for the study tests were calculated. A *P*-value of <0.05 was considered statistically significant.

Results

Table 1 describes the clinical and functional characteristics of patients included in the study.

Table 1.

The clinical and functional characteristics of the study patients.

	n (%) / M ±SD
Nr. of patients	93
Sex, M/F	62/31
Age (years), range	8.6 ± 3.1 (5-17)
Height, cm	135.5 ± 18.8
Weight, kg	33.6 ± 14.3
Age of first symptoms, years	3.4 ± 2.5
Intermittent asthma	14/93 (15.1%)
Mild persistent asthma	54 (58.1%)
Moderate persistent	25 (26.9%)
Severe persistent	0 (0.0)
Treatment	
SABA plus ICS as needed	13 (14%)
Inhaled corticosteroid, µg/day	80/93 (312.3±130.1)
Antileukotriene	12 (12.9%)
LABA	18 (19.4%)
Spirometry	
FVC, %pred	92.2 ± 14.9
FEV_1, %pred	98.9 ± 17.2
FEV_1/FVC, %pred	103.9 ± 9.7
FEE_{50}, %pred	88.3 ± 26.5
FEF_{25-75}, %pred	88.8 ± 26.9
Plethysmography	
sRaw	176.3 ± 76.0
FRC, %pred	148.8 ± 64.8
TLC, %pred	114.7 ± 30.2
RV, %pred	206.7 ± 117.7
RV/TLC, %pred	168.9 ± 54.3
FRC/TLC,%pred	131.5 ± 27.9

Air trapping was detected in 78.5% of patients according to RV data, 77.4% of patients according to RV/TLC data, 58% of patients according to FRC/TLC data, and 57% according to FRC data. Only 26.9% of patients, according to TLC, had distension (hyperinflation). Residual volume (RV) is the most sensitive parameter for detecting air trapping, and air trapping is the earliest and most sensitive functional abnormality than lung distension (hyperinflation).

We studied whether there is any relationship between air trapping (RV) and airflow obstruction (FEV_1) (Figure 1). There was no statistically significant relationship between them ($r=-0.104$, $P=0.325$). Based on their cutoff, we found three functional phenotypes. No patient has the phenotype obstructive + without air trapping, which shows that air trapping is the earliest asthma phenomenon (Figure 1).

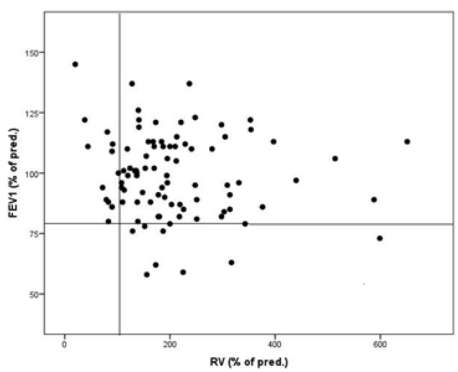

Fig. 1. Relationship between FEV_1 and RV.

We studied the relationship between RV and $FEF_{25\%-75\%}$ (plethysmographic and spirometric variables for small-airway dysfunction) and found no statistically significant correlation ($r=-0.150$, $P=0.154$) (Figure 2). A weak negative correlation ($r=-0.319$, $P<0.05$) was found between RV/TLC and FVC (Figure 3).

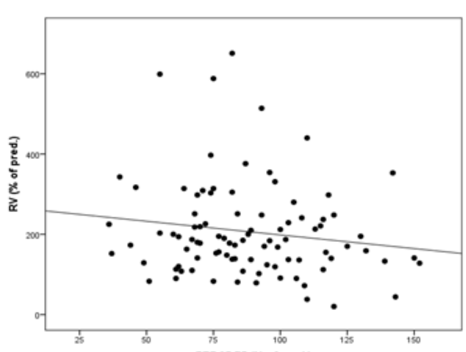

Fig. 2. Relationship between RV and $FEF_{25\%-75\%}$.

We studied the sensitivity and specificity of lung function variables (FEV_1, FVC, $FEF_{50\%}$, and sRaw) to predict the presence of air trapping (RV>140%pred) with the ROC curve. None of these variables can discriminate the presence of air trapping (Figure 4).

The relationship between RV/TLC and asthma severity was not statistically significant ($r=0.171$, $P=0.106$). A weak negative correlation was determined between RV and age ($r=-0.252$, $P=0.046$) (Figure 5). At the same time, we found a moderate positive correlation between TLC and RV/TLC ($r=0.65$, $P<0.001$).

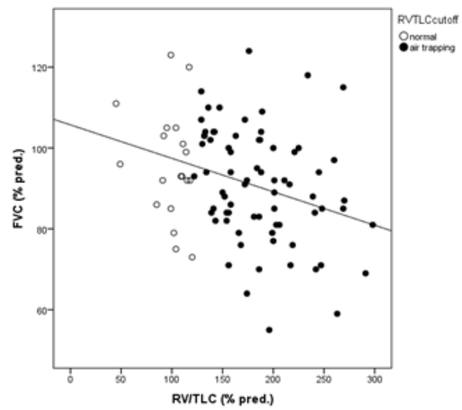

Fig. 3. Relationship of RV/TLC (%pred) with FVC (%pred).

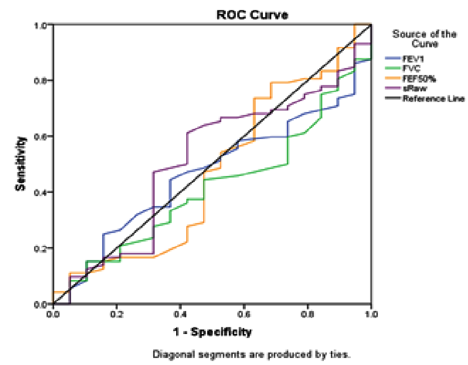

Fig .4. ROC curve for air trapping detection. For sRaw 146.5, sensitivity - 66.7%, specificity -42.1%

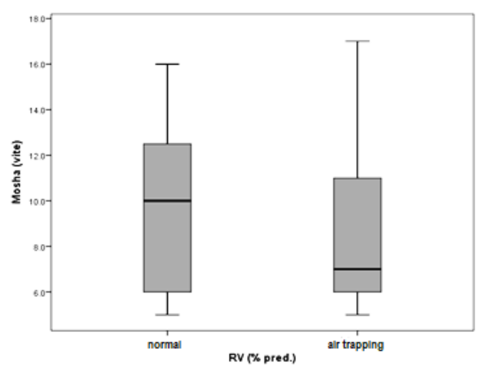

Fig. 5. Distribution of RV values with age.

We found five phenotypes of patients with air trapping (RV>140%pred):

-The first type, with increased RV, decreased FVC, and normal TLC in 12.3% of the patients, the so-called pseudo restriction phenotype.

-The second type has increased RV, normal FVC, and increased TLC in 26% of cases.

-The third type, with an increased RV, normal FVC, and normal TLC in 52% of patients.

-The fourth type, with increased RV, decreased FVC, and increased TLC in 26% of patients.

-The fifth type has increased RV, normal FVC, and decreased TLC in 1.3% of patients, which indicates that air trapping can also occur in restrictive pathology.

Discussion

Lung function assessment is an integral part of efforts to evaluate asthmatic children objectively. As shown, most children with asthma have normal FEV_1 values during disease stability.[20,21] The measurement of static lung volumes can provide important data about lung function.

According to the ATS/ERS Task Force, an increase in RV and RV/TLC is deemed a marker of small-airway closure, and therefore an air trapping marker as well.[26] Several studies about static lung volumes support this fact.[1,27-29]

In our study, 78.5% of the patients had air trapping. From the literature analysis, we found support for plethysmographic volume measurement to aid in objective asthma evaluation. Labbe et al.[30] found air trapping in 40% of children aged 5-19. The higher percentage of air trapping than reported by Labbe et al.[30] in our study was associated with the younger age of the patients (mean age of 8.6 years versus 10.67 years). We found a statistically significant negative correlation between age and air trapping (Figure 5). Furthermore, it is well-known that the caliber of distal pathways varies greatly between subjects. This anatomy leads to different functional consequences because subjects with larger distal calibers are predisposed to less airway closure.

No statistically significant relationship was found between the air trapping marker (RV) and the airflow obstruction marker (FEV_1) (Figure 1). Asthma involves the entire respiratory tract, and the distal and proximal airway involvement represents different expressions of the same disease. The reduction of the caliber of distal pathways is the most sensitive index of asthma. According to this concept, the proximal airway obstruction should be associated with distal airway involvement. Our results support this concept as children with obstruction also show air trapping. Mahut et al.[1] showed results that differ from our study; a small number of children with obstruction did not show air trapping, mainly boys with greater lung volumes, which have a bigger airway caliber and consequently lack distal closure.

Our study shows that systematic measurement of lung volumes by plethysmography is necessary for 67% of patients, as the functional spirometric variable FEV_1 cannot predict the presence of air trapping (Figure 1). Mahut et al.[1] found isolated air trapping without obstruction in 11% of children with asthma.

We did not find any significant correlation between RV (plethysmographic variable for small airway dysfunction) and $FEF_{25\%-75\%}$ (spirometric variable for small airway dysfunction) (Figure 2). In a study by Sorkness et al.,[28] $FEF_{25\%-75\%}$ did not correlate with other air trapping variables such as RV/TLC and FVC. Based on these results, we must be careful when interpreting $FEF_{25\%-75\%}$ as an indicator of small airway dysfunction. The literature supporting the validity of $FEF_{25\%-75\%}$ as an indicator of peripheral obstruction is inconclusive due to its variability and dependence on volume change.

We found a negative correlation (r=-0.319, $P<0.05$) between RV/TLC (a plethysmographic indicator of air trapping) and FVC (a spirometric indicator of air trapping) (Table 2, Figure 3). Two major studies support this result.[1,28] This confirms that FVC reduction can be considered an air trapping indicator and should be supplemented by measuring pulmonary volumes.

None of the spirometric variables (FEV_1, FVC, sRaw, and $FEF_{25\%-75\%}$) can detect air trapping (Figure 4); therefore, a plethysmographic measurement of pulmonary volumes is necessary. The relationship between RV/TLC and asthma severity was non-statistically significant, indicating that air trapping is altered at all degrees of asthma severity. Several studies on functional changes in small airways support this.[31-34]

In asthma, TLC may be elevated, normal, or decreased: 26.9% of patients present distension (TLC>120%pred), and 3.2% of patients present restriction (TLC<80%pred). The earliest functional change in asthma is the air trapping phenomenon, while distension results in only 26.9% of patients.

An increase in RV occurs according to the following phenotypes:

-The first type, with increased RV, decreased FVC, and normal TLC in 12.3% of the patients, the so-called pseudo-restriction phenotype or small airway obstruction syndrome, was also reported by other authors.[1,6,7,35] This finding indicates lung volume measurement is indicated in all cases where spirometry shows a decrease in FVC since only lung volume measurement (TLC) can confirm the presence of a restrictive process or differentiate the presence of mixed obstruction-restriction phenotypes.[36]

-The second type has increased RV, normal FVC, and increased TLC in 26% of cases.

-The third type, with an increased RV, normal FVC, and normal TLC in 52% of patients, indicates that RV increases at the expense of FRC and is not associated with alteration of either FVC or TLC in most cases.

-The fourth type, with increased RV, decreased FVC, and increased TLC in 26% of patients, indicates that RV may increase at the expense of FVC even though there is also an increase in TLC.

-The fifth type has increased RV, normal FVC, and decreased TLC in 1.3% of patients, which indicates that air trapping can also occur in restrictive pathology.

In 1973 Colp and Williams[37] first described a “restrictive pattern of ventilatory impairment” that they attributed to reversible closure of the airways. These data are not widely known and should not exclude the diagnosis of asthma, a reversibility test, or appropriate asthma therapy.[5,38,39]

Furthermore, we showed a strong statistically significant correlation between TLC and RV/TLC. This result indicates that increased distension is associated with increased air trapping phenomenon in patients with asthma.

Conclusions

Air trapping is the most common and earliest functional phenotype; thus, it is the most sensitive functional parameter for identifying functional abnormalities in asthma. It is present in all degrees of asthma severity.

Spirometric variables cannot detect small-airway obstruction syndrome (air trapping); therefore, a plethysmographic measurement of pulmonary volumes is necessary.

Functional physiological phenotypes such as air trapping, restriction, and pseudo-restriction are present in children with asthma and can only be identified by measuring lung volumes.

Ethical Considerations

The study protocol was reviewed and approved by the Ethics Committee of the University Hospital Center "Mother Tereza." Written informed consent was obtained from each participant's parent or guardian.

Competing Interests

The authors declare that they have no competing interests.

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