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To cite this article: Larissa Andrade de Sá Feitosa, Murilo Carlos Amorim de Britto, Andrea Aliverti, Jéssica Brito Noronha & Armèle Dornelas de Andrade (2018): Accuracy of optoelectronic plethysmography in childhood exercise-induced asthma, Journal of Asthma, DOI: 10.1080/02770903.2018.1424196

To link to this article: <https://doi.org/10.1080/02770903.2018.1424196>



Published online: 23 Jan 2018.



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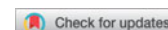
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Accuracy of optoelectronic plethysmography in childhood exercise-induced asthma

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ABSTRACT

Objective: To assess the variations of end-expiratory volume of chest wall (EEVcw) measured by optoelectronic plethysmography (OEP) as a diagnostic tool in exercise-induced asthma (EIA) among asthmatic preschool children. **Methods:** Forty children diagnosed with asthma were included in the study. Spirometry was used as a gold standard test for comparison with OEP. A 10% decline in forced expiratory volume in 1 second was considered positive for EIA. OEP was performed with 8 cameras at a frequency of 60 Hz and 89 markers were placed on the thoraco-abdominal surface of participants. Following bronchoprovocation testing on a treadmill, series of OEP and spirometry were conducted between 5 and 30 minutes after exercise. To obtain the ideal cut-off point, a receiver operating characteristic (ROC) curve was constructed for the largest EEVcw. The highest Youden index was used as criteria to obtain the cut-off point with the best sensitivity and specificity. **Results:** Of the 40 children studied, 16 had EIA. According to the ROC curve, the cut-off point of 0.185% for EEVcw provided mean sensitivity (95% confidence interval) of 93.75% (0.69–0.99), for a specificity of 83.33% (0.63–0.95), when using the largest increase in the period of 5–30 minutes post-exercise. The low area of the ROC was 0.93 (0.85–1.00) for $p < 0.001$. **Conclusion:** OEP can be accurately used to replace spirometry in asthmatic children unable to adequately execute the required manoeuvres.

ARTICLE HISTORY

Received 28 November 2017
Revised 26 December 2017
Accepted 1 January 2018

KEYWORDS

Diagnostic techniques;
respiratory system; signs and
symptoms; respiratory;
sensitivity and specificity;
respiratory mechanics and
image processing;
computer-assisted

Introduction

Exercise-induced asthma (EIA) is a disease that occurs primarily in the age range from preschool children to young adults, who are more physically active, and is a limiting factor in quality of life (1–3). It is characterized by a transient airway obstruction immediately after vigorous exercise and its main symptoms are dyspnoea, coughing, wheezing, and chest constriction (4–6).

Although EIA appears to be a common problem, it has been little investigated in the pediatric population of many countries, with research mostly focused on athletes (7–10). EIA is prevalent in 45% of asthmatics, reaching 90% in individuals with persistent asthma (10–13). Incidences are lower among children living in rural areas than those in urban regions (14). Asian children are more likely to suffer from EIA than Caucasian children, who in turn are more susceptible to it than children from other groups (15). Despite its frequency, it is difficult to diagnose. Determining accuracy in identifying cases is essential to avoid diagnostic errors and inappropriate treatment. Correct treatment promotes better control of the disease and improved quality of life.

The gold standard for EIA diagnosis is spirometry followed by exercise-based provocation, where resting values are assessed and compared with serial values from the end of exercise until 30 minutes later. A positive response occurs with a 10–15% reduction in forced expiratory volume in one second (FEV₁) after exercise (6). However, its use carries certain limitations, particularly in preschool children, since adequate execution requires patients to have a relatively complex cognitive level (16).

Optoelectronic plethysmography (OEP) is a non-invasive technique where subject cooperation is not needed to evaluate lung capacities and volumes (17). It has been used to assess healthy individuals and those with chronic obstructive pulmonary disease (COPD) during exercise (18,19). This system also enables analysis of the effects of bronchoconstriction on operating volumes in asthmatic patients (20,21), as well as dynamic hyperinflation occurring during exercise in patients with COPD (18). This instrument has been accurately applied to measure lung capacities and volumes in non-cooperative patients, such as those on mechanical ventilation (22–24) and newborns (25).

Given the need to assess non-collaborative children and for a non-invasive means of studying asthma, particularly EIA, the objective of the present study was to assess the accuracy of OEP in diagnosing EIA in asthmatic children and compare it with the gold standard, namely spirometry testing with exercise provocation.

Methods

Study population

We evaluated 45 children from the pediatric pulmonology outpatient clinic at the *Instituto de medicina Integral Prof. Fernando Figueira* (IMIP), from January to December 2011. Children aged between 6 and 12 years were included, suffering from intermittent mild to moderate persistent asthma diagnosed by a pediatric pulmonologist in accordance with Global Initiative for Asthma (26) guidelines, who satisfactorily carried out spirometry manoeuvres based on American Thoracic Society (ATS) criteria (16). In order to conduct the test, patients were not permitted to have taken short-acting Beta-2 agonists less than 6 hours before and long-acting Beta-agonists less than 12 hours prior to assessment, in addition to having been hospitalized in the last 2 weeks. We excluded children with comorbidities that would prevent participation in physical exercise, such as heart disease, neurological, and orthopedic disorders and $FEV_1 < 75\%$ of the predicted value, as a safety criteria for undertaking exercise in line with ATS norms (6).

Study design

The present study is an investigation of diagnostic accuracy based on the Standard for Reporting of Diagnostic Accuracy (27). Assessments were conducted in the Cardiopulmonary Physiotherapy Laboratory of *Universidade Federal de Pernambuco*. All the children executed 2 tests during the same time period in the morning and on the same day. First, anamneses and baseline spirometry and OEP were carried out. After exercise, OEP was performed for one minute followed by spirometry after 5, 10, 15, 20, and 30 minutes. Two independent researchers conducted the spirometry and OEP tests so that neither had any knowledge of the other's results. All researchers were appropriately trained on how to perform the tests and use the instruments in accordance with quality criteria. The study was approved by the Research Ethics Committee of the IMIP under protocol number 1829. All the parents or guardians gave written informed consent prior to assessment and participants left the laboratory once spirometric values, heart rate (HR), and peripheral oxygen saturation normalized. **Based on a pilot study**

of 30 children, sample size of 40 participants (28) was calculated according to the following formula:

$$N \equiv \frac{Z^2 * R (1 - R)}{\varepsilon^2}$$

where:

- N = sample size;
- Z = value of z which corresponds to the confidence interval;
- P = sensitivity or specificity;
- ε = margin of error (percentage points).

Values used for calculation were:

- Sensitivity = 93%;
- Specificity = 63%;
- Margin of error = 15%
- Confidence interval = 95%.

The values of sensitivity and specificity were calculated based on the end-expiratory chest wall volume (EEV_{cw}). The sample size calculated for sensitivity was 13.33 and 39.33 for specificity. A sample size of 40 patients was considered for the study.

Exercise test

Exercise testing was conducted on a treadmill (BH Fitness, Explorer, United Kingdom) in an air-conditioned environment at a temperature between 20°C and 25°C with low relative humidity (50% or less). A training session of at least 2 minutes was carried out for learning purposes at a maximum speed of 3 km/hour. An incremental protocol was applied for treadmill testing. Treadmill speed was increased in the first 2 minutes to maintain HR at around 80 to 90% of maximal HR estimated (220-age), according to guidelines for methacoline and exercise testing (6). The testing ended after 4 minutes of exercise at the estimated HR, or if requested by the child or their companion. The following parameters were measured before, during, and after the test: SpO₂ using a digital pulse oximeter (9500, Onyx, USA) and HR with a heart rate monitor (F1, Polar, Finland).

Spirometry

Spirometry was the gold standard test applied in this study, using a spirometer (Microloop 8, Micro Medical, England), in accordance with the ATS protocol (16). Participants executed manoeuvres immediately after OEP collections, while seated on a chair and using a nose clip to occlude the nostrils. Manoeuvres followed the ATS spirometry protocol (16), measuring FEV₁ and Forced Vital Capacity (FVC). Predicted values for patients followed the protocol of Pereira, specific for Brazilians (29).

A reduction in $FEV_1 > 10\%$ after exercise was considered a cut-off point for diagnosis of EIA, as per guidelines for methacoline and exercise testing (6). Calibration of the device was previously checked at the beginning of each morning.

Optoelectronic plethysmography

OEP was performed before and after exercise with an optoelectronic plethysmography system (BTS Bioengineering, Italy). The device was calibrated prior to each evaluation and assessment protocol followed the recommendations of CALA et al. (30), where 89 markers were secured to the thoraco-abdominal surface of patients with adhesive. Markers were hemispheric, 8 mm wide, and retro-reflective to infrared light. Eight cameras emitting infrared light were used to produce images, operating at a frequency of 60 images per second. Four were placed in front of the individual and four were positioned behind them. Data were processed by the OEP System program™ (BTS Bioengineering, Italy) and the parameter analyzed was EEVcw during one minute. Individuals remained seated on a stool without a backrest and their arms at their sides, with each collection recorded for one minute. Collections where coughing, sneezing, and vocalization occurred were excluded.

Statistical analysis

Data were analyzed using the Graphpad PRISMA program version 4.0. A p -value of $p < 0.05$ was considered statistically significant. Descriptive analyses were performed for all anthropometric, clinical, spirometric, and OEP data.

The Kolmogorov–Smirnov test was applied to continuous variables used in the study. The unpaired t -test and Mann–Whitney test were employed to compare groups with and without EIA when appropriate.

To obtain the ideal cut-off point, a receiver operating characteristic (ROC) curve was constructed for the largest EEVcw. Youden's index was calculated for each cut-off point on the curve. The highest Youden index was used as criteria to obtain the cut-off point with the best sensitivity and specificity. For the same cut-off point, we calculated the predictive and negative value for the index test. The value above the cut-off point considered was used to confirm a positive test result. Spearman's correlation was applied to analyze the correlation between EEVcw and FEV_1 .

Results

Of the 45 children initially assessed, 4 were excluded due to baseline $FEV_1 < 75\%$ and 1 for being unable

to adequately perform the spirometric manoeuvres (Figure 1). Of the 40 children included, 16 (40%) exhibited exercise-induced asthma. The general characteristics of the patients are shown in Table 1. A difference was recorded between the 2 groups with relation to time since the last asthma crisis, with no difference between HRs reached during exercise.

In regard to asthma severity, 18 children from the EIA group had intermittent asthma, 4 mild persistent, and 2 displayed moderate persistent asthma. In the negative EIA group, 5 children exhibited intermittent asthma, 8 mild persistent, and 3 had moderate persistent asthma. Nineteen subjects from the EIA group suffered from controlled asthma and 5 exhibited a partially controlled condition, while among negative EIA patients, 10 had controlled asthma, 4 partially controlled, and 2 uncontrolled. In subjects positive for EIA, 6 children used budesonide, 5 took beclomethasone, and 13 used no routine medication, whereas in those negative for EIA, 3 used budesonide, 3 formoterol, 5 beclomethasone, and 5 individuals took no routine medication.

The mean (95% CI) of the maximum EEVcw variation percentage in the negative EIA group after exercise was -0.36% (-0.81 – 0.098) and the greatest reduction in FEV_1 for this group was -4.30% [-6.27 –(-2.35)]. In the EIA group, EEVcw was 2.36% (1.20 – 3.52) and FEV_1 was -24.88% [-31.19 –(-18.58)]. Figure 2 shows the median of EEVcw for both the positive and negative EIA groups. A moderate correlation was observed between EEVcw and FEV_1 , with $r = -0.6625$ and $p < 0.0001$ (Figure 3).

According to the ROC curve, the cut-off point of 0.185% for the EEVcw provided mean sensitivity (CI 95%) of 93.75% (0.69–0.99) for a specificity of 83.33% (0.63–0.95) with a Youden's index of 0.77 when using the largest increase in the 5–30 minute period after exercise (Table 2). The area below the ROC curve was 0.93 (0.85–1.00) for $p < 0.001$ (Figure 4). The predictive positive value was 78.95% (54.43–93.95%) with a predictive negative value of 95.24% (76.18–99.88).

Discussion

Until completion of this investigation, the authors found no literature study that assessed the accuracy of OEP in diagnosing EIA among schoolchildren. We found that the increase in EEVcw above 0.185% between 5 and 30 minutes after exercise testing is an accurate cut-off point for diagnosing EIA in asthmatic preschool children. Given that it is a non-invasive technique and does not require patient collaboration, OEP can be an alternative in the diagnosis of EIA in non-collaborative children.

Dellacà et al. (31) studied sedated and anaesthetized patients with respiratory failure on mechanical ventilation and demonstrated that OEP is reproducible in

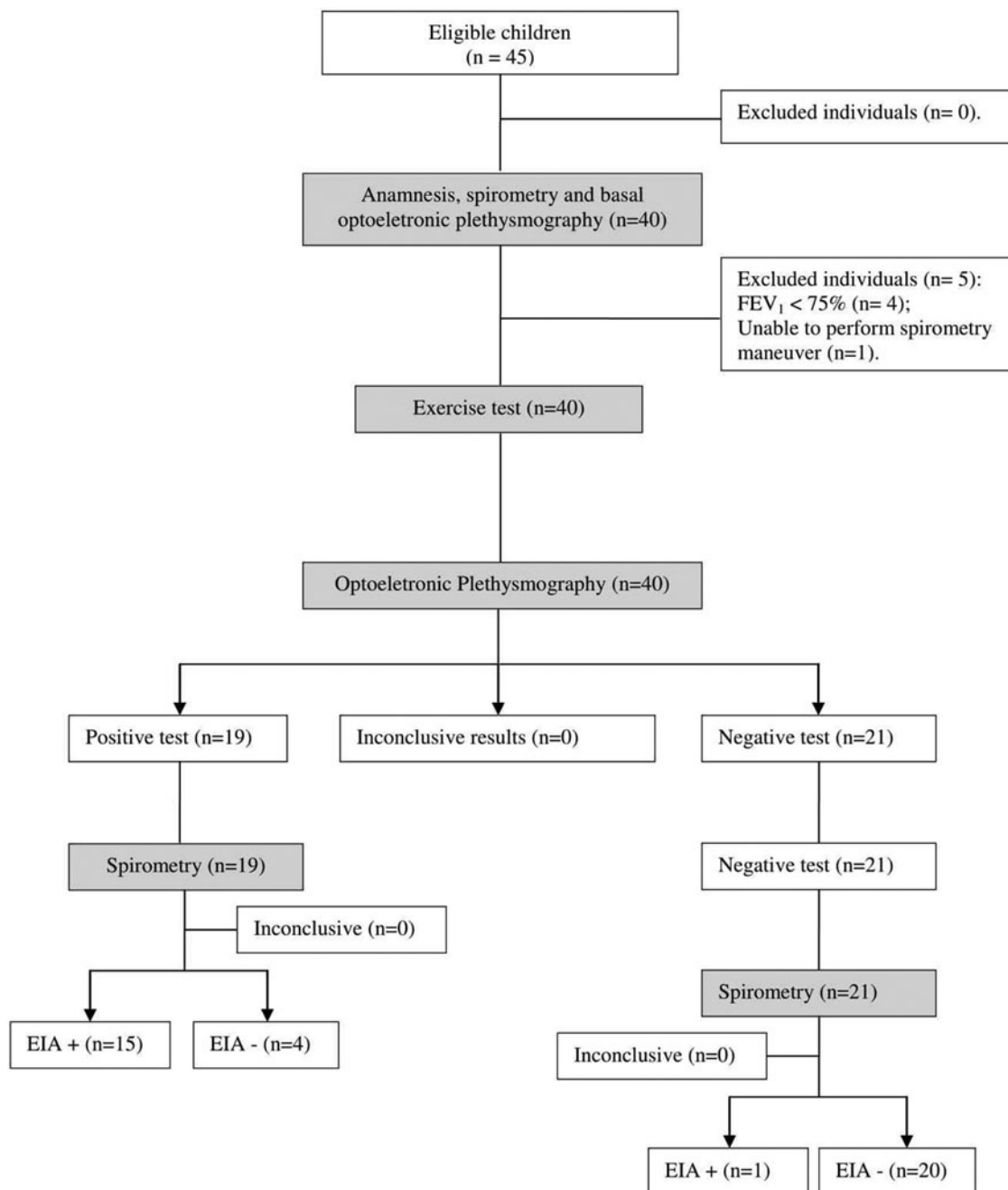


Figure 1. Flow diagram of volunteers during the study according to standard for reporting of diagnostic accuracy.

evaluating EEVcw variations resulting from changes in end-expiratory pressure of the ventilator. The author also found a strong positive correlation between EEVcw of OEP and end-expiratory lung volume recorded by the helium dilution technique. The EEVcw tends to decline during exercise to contribute to the increase in tidal volume among healthy individuals (32,33). However, in those with COPD, EEVcw tends to rise during exercise, primarily due to the limited expiratory flow in these patients (18,34). In an investigation of children with asthma, Kosmas et al. (35) reported that most of the asthmatics studied exhibited limited expiratory flow

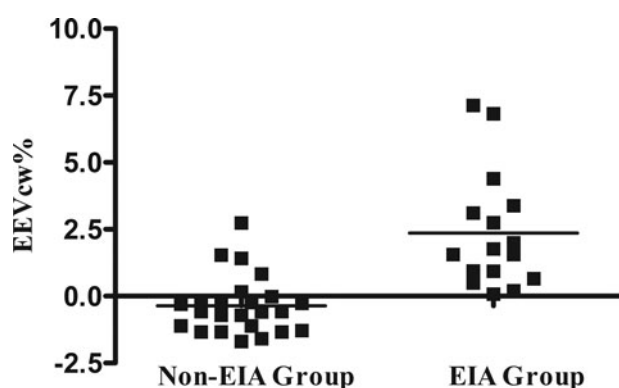
and dynamic hyperinflation when exercising, including those without EIA. According to Calverley & Koulouris (34), when expiratory flow is already limited at rest, any increase in ventilation during exercise can cause dynamic hyperinflation. The present study recorded a rise in EEVcw in the EIA group and a consequent increase in hyperinflation of the chest wall following exercise. However, those without EIA exhibited a decrease in EEVcw after exercise similar to that observed by Alivert et al. and Vogiatzis et al. (32,33) in healthy individuals.

Filippelli et al. (20) used OEP to study adults with asthma during a methacoline-induced crisis and observed

Table 1. General characteristics of non-EIA group and EIA group in asthmatic children between 6 and 12 years old.

	EIA Group ^a (n = 16)	Non-EIA group (n = 24)	p value
Age (years)	9.68 (8.46–10.91)	9.3 (8.6–10.01)	0.49
Sex (boy/girl)	11/5	15/9	—
BMI Z score	0.26 (–0.37–0.89)	0.32 (–0.09–0.73)	0.87
SpO ₂ (%)	98.73 (98.20–99.27)	98 (97.55–98.53)	0.11
Heart rate (bpm)	89.67 (84.37–94.96)	89.67 (86.46–92.62)	0.96
Weekly leisure activity	51.00 (33.49–68.51)	41.35 (30.11–52.59)	0.46
Last exacerbation (month)	6.72 (1.21–12.22)	17.75 (8.20–27.30)	0.04*
Basal spirometry			
FEV ₁ (%pred)	96.00 (88.55–103.5)	89.25 (85.08–93.42)	0.08
FVC (%pred)	100.7 (94.59–106.8)	91.58 (87.35–95.81)	0.01*
FEV ₁ /FVC	88.56 (84.27–92.85)	90.63 (87.28–93.97)	0.47
Basal optoelectronic plethysmography			
Tidal volume/weight (ml/kg)	8.85 (7.4–10.25)	9.07 (7.96–10.18)	0.80
Inspiratory time	1.29 (0.98–1.59)	1.39 (1.18–1.61)	0.30
Expiratory time	1.90 (1.64–2.18)	2.13 (1.89–2.35)	0.17
Minute ventilation	5.81 (5.05–6.56)	5.21 (4.46–5.96)	0.13
Frequency	20.58 (18.75–22.42)	18.86 (17.22–20.50)	0.16

Note. Data are presented as mean (95% CI). ^a Fall in FEV₁ >10% after exercise. EIA: Exercise-induced asthma; BMI: Body mass index; SpO₂: Saturation of peripheral oxygen; bpm: beats per minute; FEV₁: Forced expiratory volume in 1 second; pred: predicted; FVC: Forced vital capacity. *Indicates a significant difference between groups.

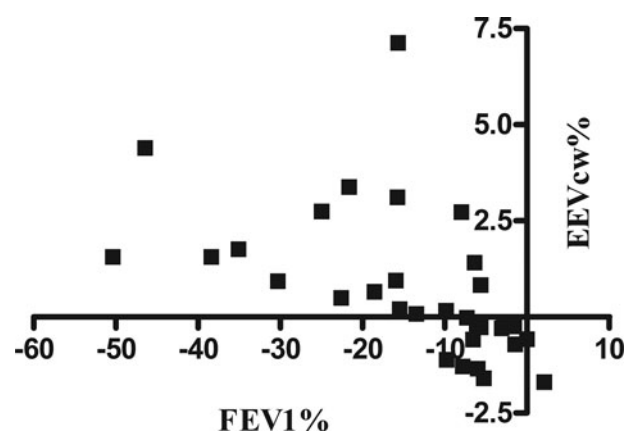
**Figure 2.** Larger increase of end-expiratory volume of chest wall (EEVcw) median in exercise-induced asthma (EIA) Group and non-EIA group after exercise test.**Table 2.** Accuracy of cut-off points for end-expiratory volume of chest wall after exercise in asthmatic children.

Cut-off points (EEVcw %)	Sensitivity % (mean 95% CI)	Specificity % (mean 95% CI)	Youden index
0.0296	100.0 (79.41–100.0)	76.18 (53.29–90.23)	0.76
0.1209	93.75 (69.77–99.84)	79.17 (62.62–95.26)	0.73
0.1850	93.75 (69.77–99.84)	83.33 (62.62–95.26)	0.77
0.3512	87.50 (61.65–98.45)	83.33 (62.62–95.26)	0.70
0.5750	81.25 (54.35–95.95)	83.33 (62.62–95.26)	0.65
0.7415	75.00 (47.62–92.73)	83.33 (62.62–95.26)	0.58
0.8781	75.00 (47.62–92.73)	87.50 (67.64–97.34)	0.63
0.9360	68.75 (41.34–88.98)	87.50 (67.64–97.34)	0.56
1.179	62.50 (35.43–84.80)	87.50 (67.64–97.34)	0.50
1.474	62.50 (35.43–84.80)	91.67 (73.00–98.97)	0.54
1.547	62.50 (35.43–84.80)	95.83 (78.88–99.89)	0.58
1.560	56.25 (29.88–80.25)	95.83 (78.88–99.89)	0.52
1.664	50.00 (24.65–75.35)	95.83 (78.88–99.89)	0.46
1.880	43.75 (19.75–70.12)	95.83 (78.88–99.89)	0.40
2.362	37.50 (15.20–64.57)	95.83 (78.88–99.89)	0.33
2.739	37.50 (15.20–64.57)	100.0 (85.75–100.0)	0.38

Note. EEVcw: End-expiratory volume of chest wall; CI: Confidence interval.

a rise in EEVcw. The authors also reported a moderate positive correlation between EEVcw and dyspnoea assessed by the Borg scale and that this parameter is superior to FEV₁ for evaluating dyspnoea (20). Gorini et al. (21) induced bronchoconstriction in asthmatic patients using histamine and reported an increase in EEVcw with OEP. However, the present study showed no correlation between increased EEVcw and reduced FEV₁, recording a moderate correlation between these 2 variables. We found that the greater the decline in FEV₁, the greater the increase in EEVcw. In other words, the more significant the obstruction of airways, the greater the retention of air in the chest wall and as such, EEVcw can be employed as an alternative parameter for assessing the obstruction of airways after exercise.

The use of asthma-specific respiratory symptom questionnaires during and after exercise has been studied as

**Figure 3.** Correlation between the variation of end-expiratory volume of chest wall (EEVcw) versus forced expiratory volume in 1 second (FEV1) after exercise.

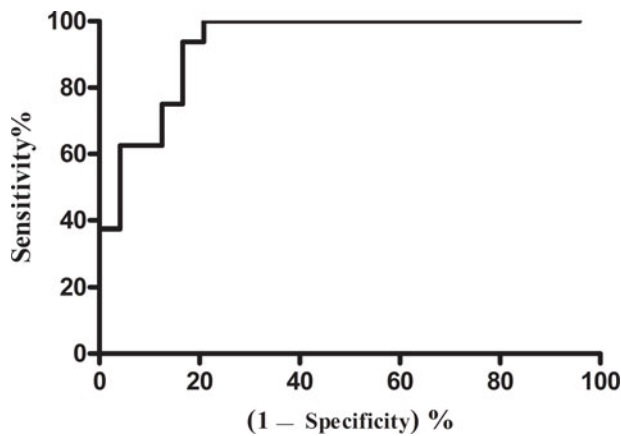


Figure 4. Receiver operating characteristic curve for end-expiratory volume of chest wall.

an alternative method to the exercise test for diagnosing EIA. This technique is inexpensive, does not require extended time periods to complete, and offers no risk to patients. **Nevertheless, several authors have demonstrated its poor accuracy and reproducibility (7,36–38).** Therefore, its use in clinical practice to diagnose EIA is not recommended.

Impulse oscillometry has been investigated as an alternative to spirometry in the evaluation of pulmonary function. By measuring pressure and flow with a pneumotachograph, it is possible to analyze respiratory system resistance and observe whether greater airway obstruction occurs following exercise. Malberg et al. (39) observed that a 30% post-exercise increase in resistance at 5 resulted in sensitivity of 62% and 94% specificity in children under 8 years old. As previously mentioned, accuracy achieved for this test was lower than that of OEP in the present study. OEP obtained sensitivity and specificity values close to 1 and can therefore be considered an accurate test to evaluate EIA in asthmatic schoolchildren.

Malberg et al. (39) recorded a value of 0.81 (0.75–0.87) for impulse oscillometry in the area below the ROC, while Lee et al. (40) reported a value of 0.755 (0.612–0.898) for this same instrument. An ROC curve area equal to 1 signifies perfect accuracy; thus, the closer to 1, the more accurate the test applied (41). As such, although impulse oscillometry enables accurate assessment of uncooperative children, OEP demonstrated greater accuracy in evaluating children of similar age.

In order to correctly perform spirometry, it is important that subjects cooperate to meet assessment quality criteria (16). Hankinson et al. (42) conducted spirometry testing in 20,627 healthy non-smokers aged between 8 and 80 years, and were obliged to exclude 13,198 individuals who were unable to satisfactorily execute at least 2 manoeuvres. In an investigation by Golshan et al. (43), of

the 4746 healthy non-smokers who performed spirometry manoeuvres, 405 were excluded for not meeting quality criteria for its execution. Given the difficulty of adequately executing spirometry manoeuvres, the test loses validity when conducted outside quality standards and the individual therefore remains undiagnosed. In such cases, OEP becomes an important instrument for accurately assessing children unable to properly carry out spirometry manoeuvres to obtain correct diagnosis.

We recorded a difference in FVC between groups with and without EIA. Despite this difference, both groups were above the range considered normal for this parameter (44). Moreover, the FEV₁/FVC ratio and FEV₁ displayed no inter-group differences and these values were also within the normal range. Thus, obstruction was not present for baseline spirometric variables (45) and as such, this divergence in FVC should not be considered as bias for results obtained in our study.

A difference was also observed between time elapsed since the last asthma crisis, with shorter periods reported by the EIA group. Lex et al. (36) found that a lack of respiratory symptoms in the 2 weeks prior to testing was a good predictor for excluding EIA. As such, our investigation excluded children with a history of acute asthma in the 2 weeks preceding the exercise test. A mean (95% CI) of 6.72 (1.21–12.22) months was recorded for the EIA group, which is sufficient to prevent an influence on results for this study.

Although the present study has shown good accuracy for OEP in diagnosing EIA, this method does have limitations. OEP is still an expensive system, its size makes it difficult to transport and results can be compromised by speaking and sudden movement. It is an excellent method for continuous assessment, as previously demonstrated in adults (18,32,46). However, the difficulty of speaking and sudden movement may compromise its use in children and should therefore only be employed in those who are unable to adequately execute spirometry manoeuvres.

Conclusion

In conclusion, the present study indicates that OEP is a viable and accurate alternative method for diagnosing EIA in 6–12 years-old children suffering from mild to moderate intermittent and persistent asthma. Nevertheless, additional studies are recommended in different populations with varying EIA prevalence, including those suffering from severe persistent forms of asthma.

Since OEP does not require as much cooperation as spirometry, is non-invasive and poses no risk to the patient, it represents a possible alternative for the diagnosis of EIA in preschool children and a prospect for future research.

Acknowledgements

The authors are grateful to Professors Andréa Lemos, Daniella Cunha Brandão, Patrícia Bezerra, and Maria Cristina Falcão Raposo for their assistance in revising the manuscript.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

Funding

Fundação de Amparo a Ciência e Tecnologia do Estado de Pernambuco (FACEPE). APQ 0154-4.08/15.

Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES)/Programa Nacional de Cooperação Acadêmica (PROCAD). 88881.068409/2014-0.

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