BRIEF REPORT

Multifrequency oscillometry for evaluating pediatric patients with exercise-induced symptoms

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ABSTRACT

Forced oscillometry (FOT) is valuable for assessing Exercise-Induced Bronchoconstriction (EIB) and bronchodilator response, but newer reference values for comparable FOT devices remain underutilized.
To compare FOT and spirometry parameters after exercise testing and bronchodilation in children reporting exercise-induced symptoms.
We measured Resistance (Rrs), its Frequency dependence (Fdep 5-19), and reactance (Xrs) at 5, 11, and 19 Hz during inspiration and expiration in 35 patients (ages 6-16). Spirometry, FeNO, blood eosinophils, and skin-prick tests were also assessed. After treadmill exercise, spirometry was repeated at 1', 5', 10', 15', and 20', and FOT at 3' and 18'. EIB was defined by a ≥10% drop in FEV_1, and bronchodilation was evaluated 15' post-salbutamol.
Fourteen patients with EIB exhibited lower functional values and higher inflammatory indices. Post-exercise, these patients had significant increases in Rrs z-scores and Fdep 5-19, along with decreases in Xrs compared to non-EIB patients. FOT changes correlated with the drop in FEV_1 and FEF_{25-75}. Bronchodilation was reflected in Rrs at 5 Hz and Xrs across all frequencies.
Multifrequency FOT effectively detects airway changes, with low frequencies key for EIB assessment and the 5-19 Hz range essential for bronchodilation evaluation.

IMPACT STATEMENT

Z-scored values and changes from device-appropriate reference points allow multifrequency FOT to detect airway alterations during EIB and bronchodilation.

KEY WORDS
Oscillometry; exercise-induced bronchoconstriction; bronchodilation; respiratory symptoms; children.

INTRODUCTION

Exercise limitations are a common concern among pediatric patients in pulmonary clinics. Some children experience symptoms exclusively during exercise, while others have broader, recurrent respiratory symptoms, affecting their participation in sports and psychosocial well-being (1). Diagnosing Exercise-Induced Bronchoconstriction (EIB) through exercise testing, particularly in suspected asthma cases, aids in diagnosis and guides clinical management (2).

Spirometry is often used to assess bronchial response after exercise (3). However, it requires forced breathing maneuvers, which may be challenging for young children. Moreover, forced expiratory maneuvers may induce bronchial relaxation in sensitive individuals, especially those with asthma, potentially skewing results (4). The Forced Oscillation Technique (FOT) offers an advantage as it is measured during normal breathing, providing reliable and repeatable data even in young children. FOT records respiratory impedance (Zrs), which consists of resistance (Rrs) and reactance (Xrs) (5). Modern devices can assess these parameters at multiple frequencies, allowing for the calculation of Frequency dependence (Fdep) and separate analyses of Rrs and Xrs during inspiration and expiration (5, 6).

Pediatric studies have shown FOT's utility in assessing EIB and bronchodilator response (BDR) (4-10). However, variation in devices, techniques, and patient populations, along with a lack of normative values, limits comparison between studies. Recently, we demonstrated that Rrs and Xrs z-scores derived from new predicted values at 8 Hz were useful in assessing EIB in children with exercise-induced symptoms (10). We hypothesized that using multifrequency z-scores could provide additional insights into EIB and BDR evaluation, potentially revealing changes that a single frequency module might miss. This study compares multifrequency FOT and spirometry parameters after exercise testing and bronchodilation in children with Exercise-Induced Symptoms (EIS).

MATERIALS AND METHODS

Subjects

This report is part of an ongoing study investigating the effects of exercise on FOT variables. Thirty-five outpatients (ages 6-16) attending our pediatric pulmonology unit at Sant'Andrea Hospital in Rome were consecutively enrolled if they reported EIS, with or without an asthma diagnosis. Participants were excluded if they had a respiratory infection in the past 4 weeks, required corticosteroids, Montelukast, or antihistamines within 10 days, or used beta-2 agonists in the last 6-12 hours. Additional exclusions included poor disease control, baseline FEV_1 <80%, poor cooperation, suspected exercise-induced laryngeal obstruction, or other exercise limitations (10). Parents provided informed consent, and the hospital's Ethical Review Board approved the study.

Study design

All assessments were completed in a single session. Parents answered a respiratory health questionnaire, and children underwent a medical exam, Skin Prick Tests (SPTs), Blood Eosinophil Counts (BECs), FOT, FeNO measurement, baseline spirometry, and an exercise challenge.

Measurements

Inflammatory biomarkers

SPTs assessed sensitization to common inhaled and food allergens, with positive and negative controls. A reaction ≥3 mm was considered positive. BECs were measured, and FeNO levels were assessed using triplicate single-breath maneuvers with constant expiratory pressure (11).

Oscillometry

Multifrequency FOT was conducted at 5, 11, and 19 Hz using a Resmon Pro Full device. Baseline measurements were performed in triplicate, with inspiratory and expiratory Rrs and Xrs values expressed as z-scores based on recent reference values (12).

Spirometry

Spirometry was performed according to ATS/ERS guidelines (13), with FEV_1 and other parameters expressed as percentages of predicted values (14).

Exercise testing

The exercise challenge involved running on a treadmill at 6 km/h with a 10% inclined until the target heart rate (220 - age) was reached (15). Post-exercise spirometry was repeated at 1, 5, 10, 15, and 20 minutes, and FOT was performed at 3 and 18 minutes. The bronchodilator response was assessed after administering albuterol. EIB was defined as a ≥10% fall in FEV1 from baseline (2, 3, 15), with changes in Rrs and Xrs calculated similarly.

Statistical analysis

Continuous variables were expressed as means ± SD. The Mann-Whitney U test was used for unpaired comparisons, and the χ^2 test with Fisher's correction for categorical variables. Spearman's rank correlation coefficients assessed correlations. Significance was set at $p < 0.05$.

RESULTS

The 35 subjects (age 6-16, M/F: 21/14) completed all measurements. EIB was observed in 14 (40%) sub-

***Table 1**. Main characteristics of patients with exercise-induced symptoms (EIS).*

	Non-EIB (n = 21)	EIB (n = 14)	P value
Gender (M/F)	11/10	10/4	0.260
Ages, years	11.5 ± 2.9	10.6 ± 2.7	0.377
Height, cm	148.7 ± 18.2	145.3 ± 16.6	0.662
BMI percentile	64.2 ± 36.6	77.9 ± 21.5	0.479
Asthma, n (%)	4 (19.0)	8 (57.1)	0.031
Therapy last 12 months, n (%)			
-Antileukotrienes	3 (14.3)	8 (57.1)	0.011
-Antihistamines	7 (33.3)	11 (78.6)	0.015
-Inhaled corticosteroids	16 (76.2)	13 (92.9)	0.366
Inflammatory biomarkers			
Atopy, n (%)	12 (57.1)	13 (92.9)	0.028
Blood eosinophils, %	4.2 ± 2.6	7.9 ± 5.2	0.077
FeNO, ppb	12.8 ± 11.8	31.9 ± 24.3	0.002
Baseline lung function			
FEV1%	107.5 ± 14.5	95.0 ± 10.5	0.013
FEV1/FVC (%)	89.5 ± 8.1	83.1 ± 6.6	0.012
FEF25-75%	104.0 ± 26.0	80.7 ± 16.6	0.013
zs-R5i	0.52 ± 0.93	1.28 ± 1.44	0.121
zs-R5e	0.91 ± 0.95	1.40 ± 1.25	0.312
zs-X5i	-0.23 ± 1.03	-0.83 ± 0.92	0.099
zs-X5e	-0.33 ± 1.45	-1.42 ± 1.31	0.017
zs-R5t	0.75 ± 0.91	1.39 ± 1.28	0.121
zs-X5t	-0.24 ± 1.11	-1.16 ± 0.93	0.012
zs-Fdep5_19	-0.02 ± 1.22	0.79 ± 1.14	0.080
Post-exercise changes			
Fall FEV1 (%)	-4.9 ± 3.0	-24.1 ± 13.6	<0.001
Fall FEF25-75 (%)	-12.6 ± 10.9	-39.9 ± 17.1	<0.001
Rise zs- R5i	0.10 ± 0.82	1.79 ± 2.33	0.010
Rise zs- R5e	0.14 ± 0.93	1.21 ± 2.02	0.138
Fall zs-X5i	-0.12 ± 1.16	-1.49 ± 1.82	0.007
Fall zs-X5e	-0.21 ± 1.33	-2.81 ± 4.85	0.138
Rise zs-R5t	0.12 ± 0.80	1.47 ± 2.22	0.086
Fall zs-X5t	-0.08 ± 1.06	-2.32 ± 3.57	0.059
Rise zs-Fdep5_19	0.14 ± 0.80	1.60 ± 1.71	0.007
Post-bronchodilator changes			
DFEV1 (%)	5.9 ± 6.7	25.1 ± 18.3	<0.001
DFEF25-75 (%)	17.3 ± 24.4	64.6 ± 44.1	<0.001
Dzs-R5t	-0.74 ± 1.01	-2.33 ± 2.14	0.008
Dzs-X5t	0.29 ± 0.78	2.09 ± 3.21	0.012
Dzs-R11t	-0.84 ± 0.92	-1.58 ± 1.28	0.055
Dzs-X11t	0.33 ± 0.51	2.46 ± 2.94	<0.001
Dzs-R19t	-0.86 ± 1.03	-0.89 ± 0.90	0.711
Dzs-X19t	0.45 ± 0.94	1.88 ± 1.75	0.002
Dzs- Fdep5_19	-0.04 ± 0.66	-2.00 ± 2.11	<0.001

EIB: exercise-induced bronchoconstriction. Inspiratory, expiratory, and total resistance (R), and reactance (X) at 5, 11, and 19 Hz (e.g., R5i, R5e, R5t, X5i, X5e, X5t). Less relevant results for baseline and post-exercise frequencies (11 and 19 Hz) are not reported.

jects, with higher atopic inflammation and lower baseline lung function than those without EIB. Low baseline z-scores of expiratory Xrs at 5 Hz better distinguished EIB patients (**Table 1**).

Post-exercise, inspiratory Rrs and Fdep 5_19 z-scores increased, and Xrs z-scores decreased more in EIB patients than those without EIB. Bronchodilator responses included reductions in Rrs and increases in Xrs across all frequencies and respiratory phases. Changes in these z-scored FOT parameters correlated with percent changes in FEV_1 and $FEF_{25\text{-}75}$ ($r = 0.58$ to 0.76, $p < 0.001$ for all). After exercise, Fdep 5_19 increased inversely with FEV_1, while Xrs decreased in direct correlation with the reduction in $FEF_{25\text{-}75}$ (**Figure 1, A, B**). Conversely, after bronchodilation, Fdep 5_19 decreased as FEV_1 increased, and Xrs increased in direct correlation with the improvement in $FEF_{25\text{-}75}$ (**Figure 1, C, D**).

DISCUSSION

Our preliminary study shows that multifrequency FOT and spirometry are useful for evaluating airway narrowing due to exercise and bronchodilation in children with Exercise-Induced Symptoms (EIS). Rather than overlapping, the results of these tests appear complementary. FOT is more effective than spirometry in identifying responses to bronchial challenges and bronchodilator responsiveness (6). This suggests a clinical role in asthma diagnosis, assessing disease control, and integrating with other biomarkers for phenotyping and monitoring patients with obstructive diseases. These include early-onset conditions such as those associated with prematurity or congenital abnormalities, comorbidities like obesity, and upper airway dysfunction. Other potential applications include reducing infectious exposure in pulmonary function laboratories by avoiding high aerosol-generating maneuvers and enabling home monitoring (16). However, FOT devices remain costly, challenging to interpret, and require further standardization, including device-specific and multiethnic reference values, before they can be widely adopted.

As expected, EIB was frequently associated with asthma and atopic inflammation, even among patients on anti-in-

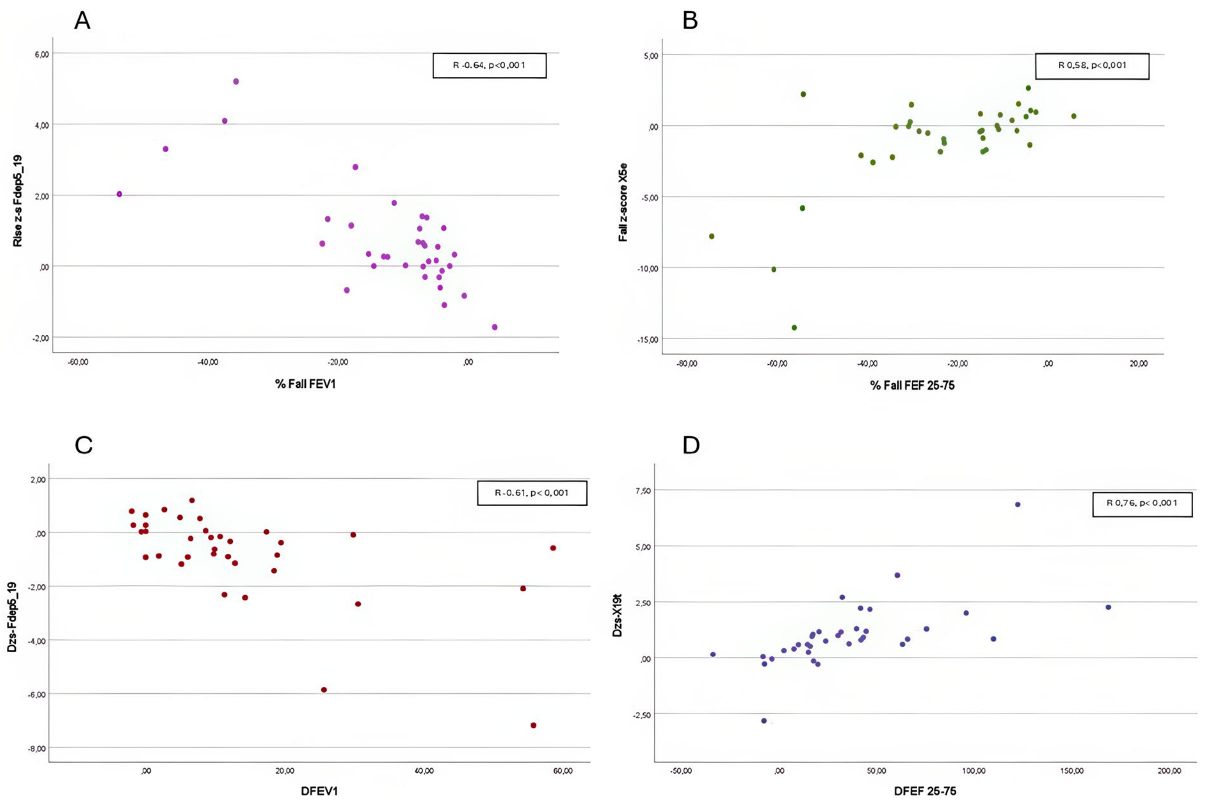

***Figure 1**. Correlations of post-exercise **(A, B)** and post-bronchodilator changes **(C, D)** in FOT parameters with respective changes in FEV1 and FEF25-75.*

flammatory therapy. Baseline spirometry and low-frequency baseline Xrs, rather than Rrs, distinguished children with EIB. Xrs becomes more negative at frequencies below 8-10 Hz in response to peripheral airway obstruction and gas trapping (17). Therefore, low Xrs z-scores could help identify children prone to EIB alongside spirometry and inflammatory biomarkers.

Our findings support the use of post-exercise changes in low-frequency inspiratory Rrs and Xrs for assessing EIB (4, 7, 10), consistent with our previous reports on changes in z-scores of 8-Hz Rrs and Xrs (10). Additionally, increased zs-Fdep 5_19 helped identify EIB, as this parameter reflects heterogeneous airway obstruction (6). High frequencies (11 and 19 Hz) poorly discriminated EIB, suggesting they are less suitable for pediatric airway assessment.

Post-bronchodilator responses showed improved airway patency through a reduction in Rrs and an increase in Xrs, independent of frequency or respiratory phase.

Limitations of this study include the small sample size and lack of healthy controls, but it represents the first phase of ongoing research in a clinical setting. Future studies could help validate our findings in specific pediatric groups experiencing exercise-induced symptoms. For example, establishing cut-offs for FOT indices in response to exercise and bronchodilators in asthmatic children with varying levels of disease control and exploring their applicability in other respiratory conditions.

In conclusion, multifrequency FOT effectively evaluates airway changes. Low frequencies during inspiration best reflect EIB, while a broader 5-19 Hz range captures bronchodilation.

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COMPLIANCE WITH ETHICAL STANDARDS

Conflict of interests

The Authors have declared no conflict of interests.

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Ethical approval

Human studies and subjects

The study adhered to the ethical standards established in the Declaration of Helsinki; participants gave written consent before enrollment.

Data sharing and data accessibility

The respiratory sound database is available for researchers upon request to the Corresponding Author.

Publication ethics

Plagiarism

Authors declare no potentially overlapping publications with the content of this manuscript and all original studies are cited as appropriate.

Data falsification and fabrication

All the data corresponds to the real.

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