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# Postexercise Airway Responses by Spirometry and Oscillometry in Nonathlete and Athlete Adolescents

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**Keywords:** adolescents | athletes | bronchial challenge | exercise | exercise-induced bronchoconstriction | forced oscillation technique | general population

## ABSTRACT

**Background:** Exercise-induced bronchoconstriction (EIB) is common among adolescents and athletes. While typically assessed with spirometry, oscillometry may offer complementary insights. This cross-sectional study examined how fractional exhaled nitric oxide (FeNO) and symptoms relate to postexercise airway responses assessed via spirometry and oscillometry, and whether these associations differ between nonathletes and athletes.

**Methods:** Subsamples from two adolescent cohorts ($N = 241$; 143 nonathletes, 98 athletes) completed questionnaires, FeNO measurements, and an EIB test using spirometry, by change in forced expiratory volume in 1 s ($\Delta FEV_1$), and oscillometry, by change in resistance and reactance at 5 Hz ($\Delta R_5$, $\Delta X_5$). Correlations were assessed using Spearman's rank; logistic regression evaluated associations between elevated FeNO and EIB; linear regression explored links between symptoms and postexercise airway responses.

**Results:** EIB was detected in 70 participants via spirometry ($\Delta FEV_1 \leq -10\%$), 81 via oscillometry ($\Delta R_5 \geq 25\%$), and 37 by both. Among nonathletes, FeNO was weakly correlated with $\Delta FEV_1$ ($r_s = -0.17$, $p = 0.04$), $\Delta R_5$ (0.35, $p < 0.001$), and $\Delta X_5$ ($-0.25$, $p = 0.005$). Elevated FeNO (> 20 parts per billion) was associated with EIB by $\Delta FEV_1$ (aOR 2.54, 95% CI: 1.05–6.12) and $\Delta R_5$ (aOR 3.05, 95% CI: 1.18–7.9). Respiratory symptoms also related to postexercise airway responses in nonathletes. In contrast, no such associations were observed in athletes.

**Conclusion:** In nonathletes, elevated FeNO and symptoms can indicate who needs EIB testing. These indicators were less predictive in athletes, emphasizing the value of objective assessment. Oscillometry was complementary to spirometry to assess EIB and a combination of methods might be more informative.

## 1 | Introduction

Experiencing airway symptoms, such as dyspnea or wheeze, in conjunction with exercise is common in adolescents [1] and is associated with negative health consequences [2]. Among adolescents and young adults participating in competitive sports, airway symptoms are more prevalent than among adolescents in the general population [3, 4]. Similar exercise-induced airway

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symptoms can be present in various conditions, for example, exercise-induced laryngeal obstruction (EILO) [5], or perhaps most commonly, exercise-induced bronchoconstriction (EIB) [6]. Thus, standardized testing is recommended as part of the clinical assessment of adolescents with exercise-induced airway symptoms [7].

Exercise-induced bronchoconstriction (EIB) is a transient narrowing of the lower airways triggered by exercise [6]. In children and adolescents, EIB prevalence is higher than in the general adult population, ranging from 3% to 35% [8]. Among elite athletes, EIB is widely observed, yet reported prevalence varies substantially depending on the type of sport, athletic environment, and diagnostic method [9]. The diagnostic approach for EIB comprises evaluation of change in airway calibre after a standardized bronchial challenge, for example, an exercise test, eucapnic voluntary hyperpnea or inhaled hypertonic agents. The post-challenge change in airway calibre is usually assessed by dynamic spirometry, where a change in forced expiratory volume in 1 s ($FEV_1$) of ≤−10% is considered positive for EIB [10]. Several studies have reported poor agreement between self-reported airway symptoms and having EIB objectively confirmed by a bronchial challenge. This discordance has been described in studies of adolescents from the general population [11, 12], but seems even more pronounced in athletes [4, 13], emphasizing the role of objective assessment of airway response to a standardized bronchial challenge.

Forced oscillations technique (FOT) is a method for measuring the mechanical properties of the respiratory system during tidal breathing. Oscillations are superimposed over the individual's spontaneous quiet breathing, assessing resistance and reactance of the airways [14]. Oscillometric indices can be valuable when diagnosing asthma in individuals with normal spirometry and are reported to be more sensitive to airway narrowing than spirometry [15]. The association between self-reported airway symptoms and oscillometric measurements is reported to be stronger compared with spirometry in both patients with asthma [16] and in the general population [17]. Oscillometric parameters as measures of postexercise airway responses have been reported to be sensitive for the detection of bronchoconstriction in asthmatic children [18, 19] and in adults with asthma [20, 21]. Oscillometry in relation to postexercise airway responses has also been evaluated in population-based groups, i.e. not clinically selected on asthma diagnosis, of adolescents [22] and in adult recreational athletes [23]. These studies report some discrepancies regarding EIB assessed by spirometry and oscillometry, as some individuals are EIB-positive by one modality and not the other.

Fractional exhaled nitric oxide (FeNO) is a type-2 airway inflammation biomarker [24]. FeNO has been associated with objectively confirmed EIB in asthmatic children [25] and in population-based studies of children and adolescents [26, 27]. However, the usefulness of FeNO as a predictor of EIB in athletes remains uncertain [28].

We aimed to study the relationships between respiratory symptoms, FeNO and postexercise airway responses measured by spirometry and oscillometry in adolescents—one group sampled from the general population and one from students attending a sports high school. We hypothesize that associations between respiratory symptoms and FeNO and EIB differ between adolescents from the general population compared with high school athletes.

## 2 | Methods

The study population ($N = 241$) comprised subsamples from two cohorts of adolescents, the ANDAS cohort sampled from the general population, and the CELADY cohort sampled from high school athletes. In these two cohorts previous studies have evaluated the prevalence of EIB [4, 12]. In both cohorts, the participants were invited to answer a questionnaire on respiratory symptoms, asthma and allergy. The randomly selected participants, stratified by self-reported exercise-induced dyspnea (EID), were invited to a clinical visit where a standardized exercise test to investigate EIB was performed. The ANDAS cohort enrolled 2309 adolescents (age 14.2 years) from the general population living in the Uppsala region, of whom 143 participants performed the EIB test with complete spirometry and oscillometry data. This cohort has previously been studied regarding oscillometry and EIB, but with another focus; analyzing changes in oscillometry after exercise in the same population, divided by the presence of EIB ($\Delta FEV_1 \leq -10\%$) and EID [22]. In the ANDAS cohort, it has previously been reported an association between elevated FeNO, using a different threshold than in the present study (> 20 parts per billion [ppb]), and EIB defined by spirometry, as well as an association between EID and EIB defined by spirometry [27]. The CELADY cohort enrolled 367 adolescent athletes (age 15.8 years) during their first year in sports high school, of whom 98 participants performed the EIB test with complete spirometry and oscillometry data. Following a selection process based on athletic performance within their respective disciplines—spanning 21 different sports—the students were admitted to the sports high school, rendering a selected population of high level student athletes, many of them pursuing a future elite career. In the ANDAS study, the sampling ratio EID: non-EID was set to 2:1, while in CELADY, the ratio was set to 1:1. The cohorts will henceforth be defined as nonathletes (sampled from the general population) and athletes (sampled from sports high school).

### 2.1 | Questionnaire

The questionnaire has previously been employed in adolescent cohorts [4, 12]

Occurrence of EID and wheeze was assessed by the following questions: "Have you in the last 12 months at one or more occasions had an attack of shortness of breath during or after exercise?" and "Have you at any time in the last 12 months had wheeze or whistling in your chest?"

Current asthma was defined as having a previous asthma diagnosis from a physician and experiencing respiratory symptoms in the past 12 months and/or having asthma treatment in the last 3 months.

### 2.1.1 | Fractional Exhaled Nitric Oxide (FeNO)

All FeNO measurements were conducted during the clinical visit for the exercise-induced bronchoconstriction (EIB) test, preceding oscillometry, spirometry, and exercise challenge.

FeNO was assessed twice at a flow rate of 50 mL/s (NIOX Vero; Circassia) following the technical guidelines outlined by the American Thoracic Society/European Respiratory Society [29]. Mean values are reported in the present paper.

### 2.1.2 | Exercise-Induced Bronchoconstriction Test

The participants were instructed to avoid vigorous physical activity, caffeine, nicotine, and heavy meals within 4 h before the test. They were also instructed to refrain from any short-acting β2-agonists 8 h before the test, long-acting β2-agonists 24 h before the test, leukotriene receptor agonists 72 h before the test and inhaled corticosteroids on the day of the test.

Baseline lung function measurements by FOT (Resmon Pro Full, Restech Srl) and spirometry (CardioPerfect dynamic spirometry; Welch Allyn) were performed before a treadmill exercise challenge. FOT, with a multifrequency signal of 5, 11 and 19 Hz, was measured in duplicates. Baseline respiratory resistance at 5 Hz ($R_5$) and respiratory reactance at 5 Hz ($X_5$) was calculated as the mean of two acceptable measurements, comprising 10 acceptable breaths. Spirometry was conducted in accordance with ATS/ERS guidelines [30], and $FEV_1$ was documented as the highest of three acceptable and reproducible manoeuvres (the two highest values within 150 mL of each other). The participants exercised for 7–8 min while wearing a nose clip and breathing dry air through a tubing system connected to a central gas container ($H_2O < 5$ mg/L, 18°C–22°C). Heart rate was monitored continuously, and the protocol required reaching 90% of the predicted maximum heart rate ((220—age) × 0.9) within the first 2 min and maintaining this level of exercise for 5–6 min. Postexercise FOT (single measurements with at least five artefact-free breaths) and spirometry (duplicate measurements) were performed at 5, 10, 15, and 30 min after exercise cessation.

EIB was defined as a decline in $FEV_1 \leq -10\%$ from baseline at any time point postexercise [10]. Similarly, an increase in $R_5 \geq 25\%$ was used as the cutoff for a positive airway response measured with FOT [21]. Investigators K. E. and H. J., who supervised all the EIB tests, were blinded to the participants' answers to the questionnaires.

## 2.2 | Statistical Methods

Shapiro–Wilks's test assessed the normality of continuous variables. Continuous variables that followed a normal distribution were expressed as means with standard deviations (SD). In contrast, those with non-normal distributions were presented as medians with interquartile ranges (Q1–Q3) or as geometric means with 95% confidence intervals (95% CI) (the last-named only for FeNO that had a skewed distribution to the right). Postexercise airway responses were defined as $\Delta FEV_1$ as % change from baseline to nadir after exercise; $\Delta R_5$ as % change from baseline to peak after exercise; $\Delta X_5$ as the change in actual values from baseline to nadir after exercise. Correlations between log-transformed FeNO and $\Delta FEV_1$, $\Delta R_5$ and $\Delta X_5$, respectively, were analyzed with Spearman's rank correlation coefficient. Logistic regression models were used to examine the associations between elevated FeNO defined as FeNO ≥ 25 ppb (as exposure) and EIB defined by $\Delta FEV_1 \leq -10\%$ and $\Delta R_5 \geq 25\%$ (as outcomes), yielding odds ratios (OR) and 95% CI. The logistic regression models were adjusted for height and sex. The relationships between wheeze and EID (as exposures) and $\Delta FEV_1$, $\Delta R_5$ and $\Delta X_5$ (as outcomes) were analyzed using linear regression models, yielding $\beta$-coefficients and 95% CI. Statistical significance was considered at $p < 0.05$.

All analyses used STATA 15.1 (College Station, TX: Stata Corp LLC).

## 3 | Results

The athletes competed in their sports disciplines at international, national, and regional levels. Within the group, 21 different sports disciplines were represented. Soccer, floorball, American football, basketball, and orienteering were the most common disciplines.

The baseline characteristics of the participants are presented in Table 1.

### 3.1 | Results from EIB Tests

A positive EIB test assessed by $\Delta FEV_1$ was detected in 48 participants out of 143 (33%) in non-athletes and in 22 participants (22%) out of 98 in athletes. When assessing EIB by $\Delta R_5$, 59 participants (41%) in non-athletes were EIB positive, while 22 athletes (22%) were EIB positive. Although there was some overlap between these two methods, a substantial number of participants were EIB-positive only by one of the methods (Figure 1). In nonathletes, 26 participants (18%) were EIB positive by both modalities. The corresponding number was 11 participants (11%) in athletes. The coefficient of variation for the duplicate measurements of $R_5$ at baseline was < 15% for all participants except for five participants in nonathletes, for whom the coefficient of variation was < 19%. Per group, the postexercise airway responses were as follows; in nonathletes, median (min, max) $\Delta FEV_1$ −6% (4, -40), $\Delta R_5$ 22% (−6, 133) and, in athletes $\Delta FEV_1$ −6% (5, −25), $\Delta R_5$ 10% (−18, 62).

### 3.2 | FeNO and Postexercise Airway Responses

In nonathletes, there were weak correlations between baseline log-transformed FeNO and postexercise airway responses measured by $\Delta FEV_1$ $\Delta R_5$ and $\Delta X_5$. No such correlations were found in athletes. Spearman's rho per group and modality are presented in Figure 2.

**TABLE 1** | Baseline characteristics of the participants.

| | Nonathletes ($n = 143$) | Athletes ($n = 98$) |
|---|---|---|
| Female, $n$ (%) | 86 (62.1) | 57 (58.2) |
| Age (years), median (Q1–Q3) | 14 (14–15) | 16 (15–16) |
| Height (cm), median (Q1–Q3) | 168 (163–175) | 172 (167–180) |
| BMI to age,[a] $n$ (%) | | |
| Overweight > + 1 SD | 29 (20.2) | 24 (24.5) |
| Normal −2SD to +1 SD | 108 (75.5) | 73 (74.5) |
| Thinness < −2SD | 6 (4.2) | 1 (1) |
| Rhinitis, $n$ (%) | 48 (33.6) | 26 (27.6) |
| Current asthma,[b] $n$ (%) | 43 (30.1) | 21 (21.4) |
| Wheeze,[c] $n$ (%) | 56 (39.2) | 34 (34.7) |
| Exercise-induced dyspnea,[c] $n$ (%) | 97 (67.8) | 41 (41.8) |
| ICS,[d] $n$ (%) | 23 (16.1) | 11 (11.8) |
| FeNO (ppb), geometric mean (95% CI) | 14.5 (13.0, 16.2) | 16.2 (14.7, 17.9) |
| Elevated FeNO (≥25 ppb), $n$ (%) | 26 (18.2) | 20 (20.4) |
| $FEV_1$% predicted,[e] mean (SD) | 92.5 ( ± 10.2) | 95.8 ( ± 10) |
| Abnormal $FEV_1$/FVC ratio,[f] $n$ (%) | 10 (6.9) | 3 (3) |
| $R_5$ ($cmH_20$*s/L), mean (SD) | 3.83 ( ± 0.76) | 2.92 ( ± 0.72) |
| Abnormal $R_5$,[g] $n$ (%) | 20 (14) | 2 (2) |
| $X_5$ ($cmH_20$*s/L), mean (SD) | −1.09 ( ± 0.44) | −0.69 ( ± 0.25) |
| Abnormal $X_5$[h] | 10 (6.9) | 2 (2) |

*Note:* Available data: All 143 participants responded to all the questions except athletes regarding ICS ($N = 93$).
Abbreviations: 95% CI, 95% confidence interval; BMI, body mass index; ICS, inhaled corticosteroid; FeNO, fractional exhaled nitric oxide; $FEV_1$, forced expiratory volume in one second; ppb, parts per billion; Q1, first quartile; Q3, third quartile; $R_5$, respiratory resistance at 5 Hz; SD, standard deviation; $X_5$, respiratory reactance at 5 Hz.
[a]Cutoffs according to World Health Organization.
[b]Self-reported physician-diagnosed with symptoms and/or medication.
[c]Self-reported symptom in the preceding 12 months.
[d]Any use in the preceding 3 months.
[e]Reference value: Global Lung Initiative.
[f]<Lower limit of normal according to Global Lung Initiative.
[g]>Upper limit of normal according to the reference equation by Ducharme.
[h]<Lower limit of normal according to the reference equation by Ducharme.

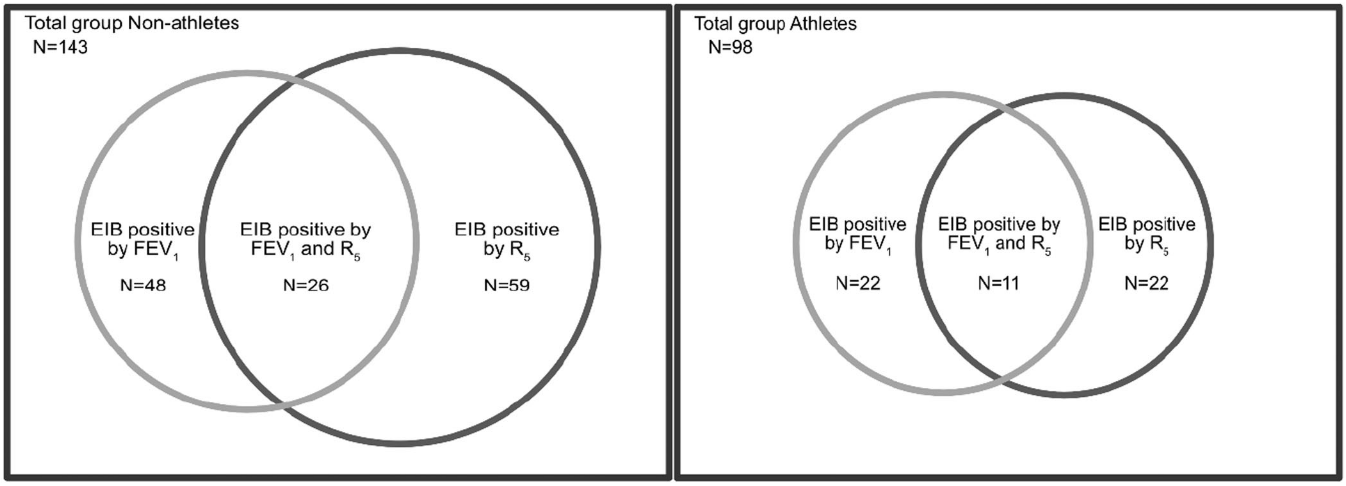


**FIGURE 1** | Proportion of participants EIB positive by $FEV_1$, $R_5$ or both methods presented per group. EIB, exercise-induced bronchoconstriction; $FEV_1$, forced expiratory volume in 1 s; $R_5$, respiratory resistance at 5 Hz.

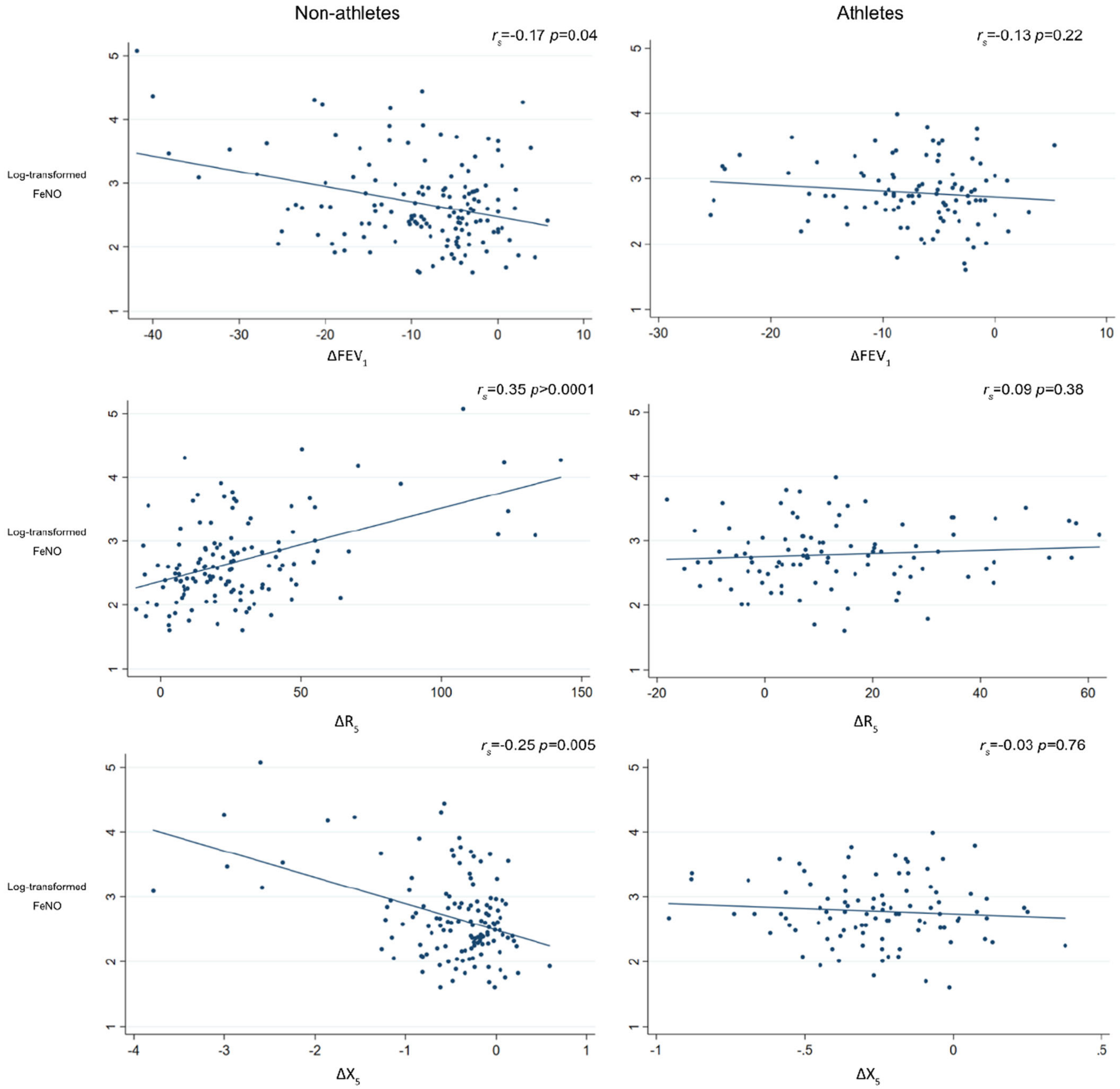


**FIGURE 2** | Rank correlation (Spearman's rho, $r_s$) between FeNO and postexercise airway response, measured by $FEV_1$, $R_5$ and $X_5$ presented per group. Nonathletes in the left column and athletes in the right column. ΔFEV1 was defined as percent change from baseline to nadir postexercise. ΔR5 was defined as percent change from baseline to peak postexercise. ΔX5 was defined as change in absolute values from baseline to nadir postexercise. 95% CI, 95% confidence interval; FeNO, fractional exhaled nitric oxide; $FEV_1$, forced expiratory volume in 1 s; $R_5$, respiratory resistance at 5 Hz; $X_5$, respiratory reactance at 5 Hz. [Color figure can be viewed at wileyonlinelibrary.com]

Furthermore, in nonathletes, there were associations between having elevated FeNO (≥25 ppb) and being EIB-positive by $\Delta FEV_1$ and $\Delta R_5$; crude OR (95% CI) 2.63 (1.12–6.17) and 2.93 (1.15–7.45). In the models adjusted for height and sex the associations remained for both $\Delta FEV_1$ and $\Delta R_5$: adjusted OR (95% CI) 2.54 (1.05–6.12) and 3.05 (1.18–7.9), respectively. In athletes, no significant associations were found between having elevated FeNO and being EIB-positive by any of the modalities (Table 2).

### 3.3 | Self-Reported Symptoms and Postexercise Airway Responses

Self-reported wheeze was associated with $\Delta FEV_1$, $\Delta R_5$, and $\Delta X_5$ in non-athletes. In contrast, in athletes, there were no associations between self-reported wheeze and postexercise airway responses by any of the modalities (Table 3).

**TABLE 2** | Association between elevated FeNO (≥25 ppb) and being EIB positive measured by $\Delta FEV_1$ and $\Delta R_5$ respectively. Reported as adjusted odd ratios and 95% confidence intervals, for all participants and stratified by group. The logistic regression models used were adjusted for height and sex.

| | Nonathletes | Athletes |
|---|---|---|
| EIB positive by $FEV_1$, aOR (95%CI) | **2.54 (1.05–6.12)** | 1.35 (95% CI: 0.41–4.44) |
| EIB positive by $R_5$, aOR (95%CI) | **3.05 (1.18–7.9)** | 2.06 (95% CI: 0.66–6.61) |

*Note:* Bold values indicate statistically significant.
Abbreviations: FeNO, fractional exhaled nitric oxide; $FEV_1$, forced expiratory volume in 1 s; PPB, part per billion; $R_5$, resistance at 5 Hz.

**TABLE 3** | Associations between self-reported symptoms and postexercise airway response measured by $\Delta FEV_1$, $\Delta R_5$, and $\Delta X_5$ respectively. Reported as $\beta$-coefficients and 95% confidence intervals, presented by group.

| | Nonathletes | | | Athletes | | |
|---|---|---|---|---|---|---|
| | $\Delta FEV_1$ | $\Delta R_5$ | $\Delta X_5$ | $\Delta FEV_1$ | $\Delta R_5$ | $\Delta X_5$ |
| Wheeze | **−4.00 (−6.91, −1.09)** | **13.92 (4.50, 23.34)** | **−0.38 (−0.61, −0.15)** | 0.46 (−2.20, 3.13) | −0.36 (−7.85, 7.13) | −0.03 (−0.13, 0.08) |
| EID | **−4.65 (−7.65, −1.64)** | 7.68 (−2.50, 17.86) | −0.21 (−0.46, 0.03) | 0.35 (−2.18, 2.88) | 1.69 (−5.53, 8.90) | −0.03 (−0.13, 0.07) |

*Note:* $\Delta FEV_1$ was defined as percent change from baseline to nadir postexercise. $\Delta R_5$ was defined as percent change from baseline to peak postexercise. $\Delta X_5$ was defined as change in absolute values from baseline to nadir postexercise. Bold values indicate statistically significant.
Abbreviations: EID, exercise-induced dyspnea; $FEV_1$, forced expiratory volume in 1 s; $R_5$, resistance at 5 Hz; $X_5$, reactance at 5 Hz.

In nonathletes, self-reported EID was associated with $\Delta FEV_1$ but not $\Delta R_5$ or $\Delta X_5$. In athletes, no associations were found between EID and postexercise airway responses by any of the modalities (Table 3).

## 4 | Discussion

In this study of postexercise airway responses measured by spirometry and oscillometry in nonathlete and athlete adolescents, we found a substantial number of participants being EIB-positive by one of the modalities. However, both groups had only a modest overlap between EIB defined by spirometry and oscillometry. In nonathletes but not in athletes, FeNO and self-reported respiratory symptoms were associated with postexercise airway responses measured by spirometry and oscillometry. Only in nonathletes did elevated FeNO increase the likelihood of being EIB-positive as determined by spirometry or oscillometry.

Baseline FeNO, $\Delta FEV_1$, and $\Delta R_5$ showed weak significant correlations among nonathletes, while no correlations were observed in athletes. To our knowledge, this is the first population-based study to investigate FeNO and postexercise airway response, measured by both spirometry and oscillometry. In children with asthma or with a high risk of asthma, baseline FeNO has been reported to correlate with postexercise airway response measured by $\Delta FEV_1$ [26]. Previous studies of FeNO and postexercise oscillometric indices are scarce. Our results indicate that FeNO is associated with the magnitude of bronchoconstriction measured by both modalities, but only in nonathletes. Similar to the nonathletes in this study, Malmberg and colleagues have reported a relationship between FeNO and severity of EIB assessed by oscillometry in young wheezy children [31].

When analyzing elevated FeNO ( ≥ 25 ppb) as a predictor for EIB, elevated FeNO was associated with EIB defined by both spirometry and oscillometry only in nonathletes. In athletes, elevated FeNO was not associated with EIB defined by any of the modalities. It has been reported previously that FeNO can predict EIB defined by spirometry in schoolchildren with asthma or suspected asthma [25], while in athletes, the value of elevated FeNO as a predictor of EIB is reported to be low [28]. In contrast, in a recent study of adolescent athletes, Goossens et al. found that elevated FeNO was an independent predictor of EIB and that FeNO levels were correlated with the severity of EIB in atopic athletes [32]. These findings suggest that different underlying mechanisms may contribute to EIB in atopic versus non-atopic athletes. Indeed, differences in the EIB phenotype, type-2 or non-type-2 inflammation, may account for the discordance between the two groups in the present study. Previous research has shown that a large proportion of athletes with EIB have non-type-2 inflammation and hence a low expected FeNO [33] whereas EIB has been connected to type-2 inflammation in the general population [34].

In nonathletes, reporting wheeze was negatively associated with $\Delta FEV_1$ and $\Delta X_5$, and positively associated with $\Delta R_5$. EID was negatively associated with ΔFEV1 in the same group, but no associations were found between EID and the oscillometric indices. This observation implies that wheeze may be linked to a more pronounced postexercise response in the peripheral airways, detected only by oscillometry. In line with this, oscillometric indices have previously been reported to relate to respiratory symptoms in individuals with normal spirometry in a large population-based middle-aged cohort [17]. In athletes, we found no associations between wheeze or EID and either modality. In children and adolescents referred for evaluation of exertional dyspnea [35] and in several studies of athletes [13] self-reported symptoms have been reported to be poor predictors of EIB measured by $\Delta FEV_1$. Our results suggest that postexercise airway responses measured by oscillometry display a similar pattern as spirometry, showing some associations in non-athletes and no associations with symptoms in athletes. This underscores that a diagnosis of EIB should not be based on self-reported respiratory symptoms alone, without objective evidence of bronchoconstriction after an airway challenge [6].

EIB defined by $\Delta FEV_1$ and $\Delta R_5$, respectively, showed a modest overlap in these two cohorts. About half of the participants who were positive by ΔFEV1 were also positive by ΔR5, while less than half of the participants who were positive by ΔR5 were also positive by $\Delta FEV_1$. Although the two methods are measures of airway obstruction, the measurements are performed at different lung volumes and may reflect changes at different levels of the respiratory system, thus perhaps recognizing different subtypes of EIB [36]. The modest overlap between $\Delta FEV_1$ and $\Delta R_5$ for diagnosing EIB is in line with previous studies in adult athletes [23], and in a previous study by our group in adolescents [22]. In contrast, in individuals with asthma or with suspected asthma, post-challenge oscillometric indices have been reported to show high agreement with EIB defined by $\Delta FEV_1$ [19–21]. Differences in population selection, severity of bronchoconstriction, and diagnostic thresholds may account for the diverging results.

The diagnostic thresholds for EIB applied in the present study were $\Delta FEV_1 \leq -10\%$ or $\Delta R_5 \geq 25\%$ at any time point postexercise. The threshold for $\Delta FEV_1 \leq -10\%$ is widely accepted for diagnosing EIB after an exercise challenge [10], while robust recommendations for corresponding thresholds for $\Delta R_5$ are scarce, and cutoff values ranging from 14% to 50% have been suggested in previous studies [18, 21, 23]. Given the broad range of the suggested cutoff values postexercise, the threshold of $\Delta R5 \geq 25\%$ used in the current study is also informed by earlier research on the oscillometric response to various bronchial challenges and bronchodilator treatments. Schulze and colleagues reported that a 45% increase in R5 was associated with a 20% reduction in $FEV_1$ during a methacholine challenge [37]. Similarly, Oostveen and colleagues found that a 32% decrease in R5 indicated a significant bronchodilator response in adults aged 18–80 years [38], a result consistent with the findings by Johansson and colleagues, where a 29% decrease in R5 was found to be a significant bronchodilator response in middle-aged adults [39].

## 5 | Strengths and Limitations

The strengths of this study include the random selection of participants from two relatively large adolescent population-based study cohorts, the standardized objective exercise challenge using dry air, and the postexercise airway responses measured by both spirometry and oscillometry.

Yet, there are some limitations that need to be addressed. Wheeze and EID were self-reported in a questionnaire, and the participant's interpretation of the questions might have affected their answers. Information on atopic status would have been of value to describe the study population further. Oscillometry was performed before spirometry at each time point, but an influence on bronchial tone by the forced expirations during spirometry cannot be completely ruled out. Due to frequent measurements and short time intervals between each measurement, single oscillometry measurements were performed postexercise, although triplicate measurements are recommended. However, in epidemiological research, one measurement has been proposed to suffice [40].

## 6 | Conclusion

For adolescents who are not high-level athletes, elevated FeNO or reports of wheezing or EID may guide clinicians in selecting those who should be referred for EIB testing. In contrast, for adolescent athletes, FeNO levels and reports of wheezing or EID appear to offer limited guidance, making access to objective testing essential.

Spirometry and oscillometry for assessing exercise-induced bronchoconstriction do not perfectly align, suggesting that the two methods may detect different locations of airway narrowing. Therefore, oscillometry could serve as a complementary tool to spirometry when evaluating abnormal airway responses after exercise. However, further research is needed to establish appropriate diagnostic thresholds for postexercise responses by oscillometric indices and the added clinical value.

### Author Contributions

**Karin Ersson:** investigation, writing – original draft, data curation, methodology, project administration, formal analysis, visualization, writing – review and editing. **Kjell Alving:** conceptualization, writing – review and editing, resources, methodology. **Margareta Emtner:** writing – review and editing, conceptualization. **Christer Janson:** writing – review and editing, resources, conceptualization. **Henrik Johansson:** writing – review and editing, conceptualization, supervision, data curation, investigation, funding acquisition, methodology. **Andrei Malinovschi:** conceptualization, funding acquisition, methodology, supervision, resources, writing – review and editing, investigation, software.


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### Ethics Statement

All participants signed a written informed consent form at inclusion in the study. For participants under 15, informed consent was also obtained from all guardians. The ethical review board in Uppsala, Sweden, provided ethical approval for this study (Dnr 2011/413 and Dnr 2016/169).

### Conflicts of Interest

Kjell Alving reports receiving personal payment, equipment, and material for a clinical study outside of the present manuscript from NIOX. Andrei Malinovschi has received lecture and/or advisory board fees from Boehringer Ingelheim and Chiesi outside the submitted study as well as in-kind support in form of nitric oxide sensors from NIOX (a producer of FeNO devices) within a frame of an investigator-initiated study (not the present study). The other authors declare no conflicts of interest.

## Data Availability Statement

The ethical approval does not allow the authors to make all the data publicly available, according to Swedish law. Unidentified data that supports the findings of this study are available upon reasonable request from the authors.

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