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# A longitudinal study of exercise-induced bronchoconstriction and laryngeal obstruction in high school athletes

Karin Ersson<sup>1,2</sup>  | Elisabet Mallmin<sup>3</sup> | Leif Nordang<sup>3</sup> | Andrei Malinovski<sup>1</sup> | Henrik Johansson<sup>1,2,4</sup>

<sup>1</sup>Department of Medical Sciences, Clinical Physiology, Uppsala University, Uppsala, Sweden

<sup>2</sup>Department of Women's and Children's Health, Physiotherapy, Uppsala University, Uppsala, Sweden

<sup>3</sup>Department of Surgical Sciences, Otorhinolaryngology and Head & Neck Surgery, Uppsala University, Uppsala, Sweden

<sup>4</sup>Department of Medical Sciences, Respiratory-, Allergy- and Sleep Research, Uppsala University, Uppsala, Sweden

## Correspondence

Karin Ersson, Department of Medical Sciences, Clinical Physiology, Uppsala University, 751 85 Uppsala, Sweden.  
Email: [karin.ersson@medsci.uu.se](mailto:karin.ersson@medsci.uu.se)

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**Background:** Exercise-induced bronchoconstriction (EIB) and exercise-induced laryngeal obstruction (EILO) are common in elite athletes. Knowledge of which factors are related to incident EIB and EILO is limited. The aim of this study was to explore the course of EIB and EILO in adolescent athletes over a 2 years period and baseline characteristics related to incident EIB.

**Methods:** Questionnaire data on respiratory symptoms, asthma, and aeroallergy and results of objective EIB and EILO tests were collected from 58 participants (27 tested for EILO) at baseline and after 2 years (follow-up). Associations between incident EIB and baseline asthma-like symptoms, exercise-induced symptoms, fractional exhaled nitric oxide (FeNO), aeroallergy, and sex were assessed using logistic regression models.

**Results:** Ten participants had incident EIB, and eight participants had persistent EIB. Five were EIB positive at baseline but negative at follow-up, while 35 participants were EIB negative at both time points. Having incident EIB was associated with reporting waking up with chest tightness (OR = 4.38; 95% CI: 1.06, 22.09). Reporting an increased number of asthma-like symptoms increased the likelihood of incident EIB (OR = 2.78; 95% CI: 1.16, 6.58). No associations were found between exercise-induced symptoms, FeNO, aeroallergy, or sex and incident EIB. Incident EILO was found in three and persistent EILO in two of the 27 participants tested.

**Conclusion:** Two in nine had incident EIB and one eighth had incident EILO, suggesting that recurrent testing for EIB and EILO may be relevant in young athletes. Particularly, EIB-negative athletes reporting multiple asthma-like symptoms could benefit from recurrent EIB testing.

## KEYWORDS

adolescent, athletes, bronchoconstriction, cohort, epidemiology, exercise-induced, laryngeal obstruction

## 1 | INTRODUCTION

Exercise-induced respiratory symptoms, such as wheeze, dyspnea, and chest tightness, are common among adolescents,<sup>1</sup> but even more common among elite adult athletes and early career athletes.<sup>2–4</sup> Some nociceptive respiratory sensations in association with intense exercise can be considered physiologically normal but may indicate underlying pathological respiratory conditions.<sup>5</sup>

Exercise-induced bronchoconstriction (EIB), a transient reversible narrowing of the lower airways provoked by exercise, is common among individuals with asthma but also occurs in individuals without an asthma diagnosis.<sup>6</sup> The prevalence of EIB in elite athletes is 20%–70%,<sup>7</sup> higher than in the general population (5%–20%).<sup>8</sup> The prevalence of EIB is higher among young athletes than among adolescents in the general population.<sup>4</sup> To identify EIB, an indirect bronchial challenge, such as exercise, hyperpnea of dry air, or inhalation of a hyperosmolar agent followed by serial lung function measurements, is recommended.<sup>6,9</sup> Exercise-induced laryngeal obstruction (EILO), a narrowing of structures of the larynx at the glottic or supraglottic level during exercise, is more prevalent in athletes than in the general population.<sup>4,10</sup> As EILO and EIB can present with similar clinical symptoms, objective testing is needed to distinguish between them. A continuous laryngoscopy exercise (CLE) test is recommended for the assessment of EILO.<sup>11</sup>

Identifying EIB is important, given its potential impact on health and performance.<sup>12</sup> However, there is a weak relationship between the presence of symptoms and objective evidence of EIB in athletes.<sup>3,13,14</sup> EIB may be over- or underdiagnosed based on exercise-induced symptoms alone due to the high prevalence of respiratory symptoms reported by athletes on the one hand and the high proportion of asymptomatic athletes presenting with evidence of EIB when screened, on the other.<sup>2,15,16</sup> Therefore, objective testing should be performed to confirm EIB.<sup>3,4,6</sup>

Currently, knowledge about the natural course of EIB and EILO in athletes is limited. There is one report of high incidence of EIB in triathletes.<sup>17</sup> Regarding EILO, one study has found that among adolescents with supraglottic EILO, receiving either conservative or surgical treatment, laryngeal obstruction persisted in a majority of those receiving conservative treatment when re-assessed by CLE test after 2–5 years.<sup>18</sup>

Screening for EIB in adolescent athletes has been suggested,<sup>4,15</sup> but the appropriate timing and selection approach are unknown. Predictors of EIB development in adolescent athletes could provide valuable information supporting clinicians in deciding who and when to test for EIB.

### Key Message

Incident EIB and incident EILO were common in this cohort of high school athletes, suggesting that recurrent testing of young athletes may be relevant. Reporting multiple asthma-like symptoms was positively associated with incident EIB, hence questions about asthma-like symptoms may be of value as part of a clinical algorithm supporting the selection of athletes to be referred for objective testing for EIB.

We aimed to study the course of EIB and EILO in a population of young athletes in years 1–3 at sports high school. Further, we aimed to study which baseline characteristics are related to the development of EIB in this population.

## 2 | METHODS

### 2.1 | Study population

In 2016 and 2017, students starting at a sports high school in Uppsala, Sweden were invited to participate in the study ( $n = 549$ ). The recruitment procedure has been described previously.<sup>4</sup> In short, the participants answered a questionnaire about respiratory symptoms, asthma, and allergy. A random sample ( $n = 98$ ) was invited to two clinical visits, first an EIB test and then a CLE test (baseline). In 2018 or 2019, during their third year in sports high school, the participants were invited to once again answer the questionnaire and repeat the EIB and CLE tests (follow-up). All data collection at baseline and follow-up was done in September–November of the respective years.

### 2.2 | Questionnaire

The questionnaire was based on the International Study of Asthma and Allergy in Childhood Questionnaire<sup>19</sup> and the European Community Respiratory Health Survey.<sup>20</sup> It has previously been used in adolescent populations.<sup>1</sup>

Occurrence of the following asthma-like symptoms<sup>21</sup> was assessed for the preceding 12 months: wheezing or whistling, waking up with a feeling of chest tightness, attacks of shortness of breath during daytime rest, and attacks of shortness of breath in the night-time.

Current asthma was defined as ever having been diagnosed with asthma by a physician, in combination with reporting symptoms during the preceding 12 months and/or having asthma treatment (excluding single therapy with short-acting  $\beta_2$ -agonists) in the preceding 3 months.

Exercise-induced respiratory symptoms<sup>1</sup> were defined as any of the following, during, or directly after exercise within the preceding 12 months: wheeze or whistling in chest, tightness in chest, an attack of shortness of breath, cough, tightness in throat, choking sensation, hoarseness, and noise during inspiration.

Aeroallergy was defined as reported cough, shortness of breath, wheeze, and tightness in chest, sneezing, blocked or runny nose, and/or irritated or watery eyes after exposure to furry animals or pollen.

Participants also reported their average time spent exercising per week.

## 2.3 | Fractional exhaled nitric oxide

Fractional exhaled nitric oxide (FeNO) was measured in duplicate at a flow rate of 50 mL/s (NIOX Vero; Circassia) in accordance with American Thoracic Society/European Respiratory Society (ATS/ERS) technical standards.<sup>22</sup> All FeNO measurements were performed during the clinical visit for EIB test, before spirometry, and exercise challenge.

## 2.4 | EIB test

Prior to EIB testing, the participants were instructed to withdraw any short-acting  $\beta_2$ -agonists 8 h before the test, long-acting  $\beta_2$ -agonists 24 h before the test, and leukotriene receptor agonists 72 h before the test. The participants were instructed not to use inhaled corticosteroids on the day of their test as well as to avoid vigorous exercise, heavy meals, nicotine, and caffeine 4 h before their EIB test. The protocol for the EIB test has been described in detail previously.<sup>4</sup> Briefly, FEV<sub>1</sub> measurements (Welch Allyn SpiroPerfect; Hillrom Inc.) were conducted as recommended in ATS/ERS standards<sup>23</sup> and forced expiratory volume in the first second (FEV<sub>1</sub>) was followed for up to 60 min after a standardized exercise challenge of 7–8 min of running on a treadmill while breathing medical air ( $H_2O < 5$  mg/L, 18–22°C). Heart rate was monitored continuously using a heart rate monitor (Polar RCX5; Polar Electro OY). The protocol required reaching a heart rate of 90% of the predicted maximum ( $(220 - \text{age}) \times 0.9$ ) within the first 2 min and maintaining this level throughout the test. EIB was defined as a decrease in FEV<sub>1</sub> of  $\geq 10\%$  compared with baseline at any time point.<sup>24</sup>

## 2.5 | CLE test

The CLE test was performed 3–51 (median 12) days after the EIB test. The procedure for the CLE test has been described in detail previously.<sup>4</sup> Laryngeal obstruction at glottic and supraglottic levels was graded 0–3. A positive CLE test, consistent with EILO, was defined as obstruction of grade  $\geq 2$  at the glottic and/or supraglottic level.<sup>11</sup>

## 2.6 | Statistical analyses

Participants who were EIB negative at baseline but positive at follow-up were defined as having incident EIB. Participants who were EIB negative on both occasions were defined as EIB negative. Participants who were EIB positive on both occasions were defined as having persistent EIB, whereas those who were EIB positive at baseline but negative at follow-up were defined as having EIB remission. The same pattern was used in the definitions of EILO.

To check the normality of the data for continuous variables, Shapiro–Wilks test was used. Normally distributed continuous variables are presented as arithmetic means with standard deviations (SD) and nonnormally distributed continuous variables are presented as medians with first quartile (Q1) and third quartile (Q3) or as geometric mean with 95% confidence interval (95% CI). Depending on data distribution between-group differences in continuous variables were tested by Kruskal–Wallis test by ranks or one-way ANOVA. Post-hoc analysis after ANOVA was performed by Tukey's method. In categorical variables, differences between groups were tested by Fisher's test. Associations between asthma-like symptoms and exercise-induced symptoms, self-reported aeroallergy, log-transformed FeNO, sex (exposures), and incident EIB (outcome) were assessed using logistic regression models estimating odds ratios (OR) and 95% CI. Similarly, we investigated the association between a number of reported asthma-like symptoms and exercise-induced symptoms at baseline (exposure) and incident EIB (outcome). Values of  $p < 0.05$  were considered statistically significant.

Due to the high dropout rate for CLE tests at follow-up, no statistical analyses were performed regarding EILO.

All analyses were done using STATA 15.1 (College Station, TX: StataCorp LLC).

## 3 | RESULTS

### 3.1 | Exercise-induced bronchoconstriction

Among 98 (58% females) participants tested for EIB at baseline, 58 (60% females) performed the EIB test at

follow-up. Participation and loss to follow-up for EIB tests during the study are shown in Figure 1.

The group that did not participate in the EIB test at follow-up ( $n=40$ ) did not differ significantly from the tested group with regard to lung function, current asthma, use of asthma medication, number of positive EIB tests, or training hours/week at baseline (Table S1).

### 3.2 | Characteristics of the study population

The characteristics of the 58 participants at baseline and follow-up are displayed in Table 1, grouped by the result of the EIB test at follow-up.

In total, 18 participants were EIB positive at follow-up, of whom 10 had incident EIB and eight had persistent EIB. Incident EIB was thus found in 10 out of 45 participants (22%). Out of the 40 participants with a negative EIB test at follow-up, five had EIB remission, and 35 were EIB negative. There was no significant difference between the incident EIB and EIB-negative groups regarding the change in FEV<sub>1</sub> during the EIB test at baseline. The changes in FEV<sub>1</sub> during the EIB test at baseline and follow-up are shown in Figure 2.

In total, 43% of the study population reported having one or more asthma-like symptoms at baseline, whereas 78% reported having one or more exercise-induced symptoms. The participants' self-reported asthma-like symptoms and exercise-induced symptoms at baseline are presented in Table 2.

### 3.3 | Sports disciplines and exercise levels

The participants were competing at the international, national, or regional level. In addition to extracurricular competing and training, the participants had curricular activities in their sports discipline 3–5 days/week. The participants reported similar median exercise levels (12.5 h/week) at each time point (Table 1). Nineteen different sports disciplines were represented, the most common being soccer, floorball, and basketball. Only two participants specialized in winter sports (alpine skiers) and none specialized in aquatic sports.

### 3.4 | Factors related to incident EIB

Having incident EIB was associated with reporting waking up with chest tightness: OR (95% CI) 4.38 (1.06, 22.09). An increased number of asthma-like symptoms related to

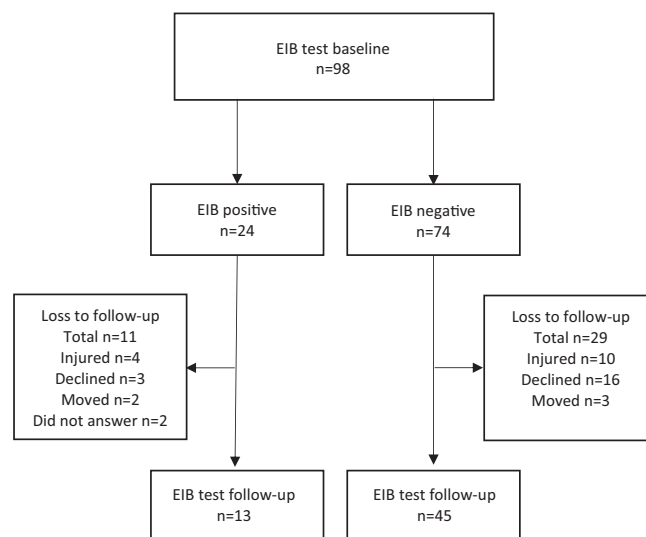


FIGURE 1 Participation and loss to follow up during the study. EIB, exercise-induced bronchoconstriction.

incident EIB (Table 3). The associations between asthma-like symptoms at baseline and incident EIB are presented in Table 3.

There were no associations between any of the exercise-induced symptoms or a number of exercise-induced symptoms at baseline and incident EIB (Table 3). Neither self-reported aeroallergy, FeNO at baseline, nor sex was related to incident EIB.

### 3.5 | Exercise-induced laryngeal obstruction

Among 75 participants (65% female) who underwent the CLE test at baseline, 27 (66% female) performed the test at follow-up. Participation and loss to follow-up are presented in Figure 3.

Results from the CLE test at baseline and follow-up are shown in Table 4. Three participants out of 24 (12%) had incident EILO. Three participants with EILO at baseline performed the CLE test at follow-up, whereof two had persistent EILO, and one had EILO remission. The participants who had incident EILO were all classified as having supraglottic EILO. One participant had both a positive EIB test and a positive CLE test at baseline (glottic EILO). That participant had EILO remission, but persistent EIB at follow-up. The two participants with persistent EILO were classified as supraglottic at both time points.

## 4 | DISCUSSION

In this two-year longitudinal study of athletes in sports high school, incident EIB was found in 10 participants



**TABLE 1** Baseline characteristics of all participants who performed the EIB test at follow-up, grouped by the result of EIB test at follow-up.

|  | Incident EIB     | Persistent EIB  | EIB remission        | EIB negative     |
|--|------------------|-----------------|----------------------|------------------|
| Participants, <i>n</i>   | 10               | 8               | 5                    | 35               |
| Age follow-up, median (Q1–Q3)                                      | 18 (17–18)       | 18 (18–18)      | 18 (18–18)           | 18 (18–18)       |
| Female, <i>n</i> (%)   | 7 (70)           | 6 (75)          | 4 (80)               | 18 (51)          |
| FVC predicted <sup>a</sup> baseline, %, mean (SD)                  | 96 (±10)         | 95 (±10)        | 88 (±7) <sup>d</sup> | 101 (±8)         |
| FEV <sub>1</sub> predicted <sup>a</sup> baseline, %, mean (SD)     | 94 (±12)         | 95 (±10)        | 93 (±7)              | 100 (±9)         |
| FEV <sub>1</sub> /FVC ratio, mean (SD)                             | 0.85 (±0)        | 0.88 (±0.1)     | 0.92 (±0)            | 0.87 (±0.1)      |
| FeNO <sub>50</sub> baseline, ppb, geometric mean (95% CI)          | 18 (13, 24)      | 19 (14, 24)     | 20 (12, 35)          | 16 (13, 19)      |
| Current asthma baseline <sup>b</sup> , <i>n</i> (%)                | 1 (10)           | 2 (25)          | 1 (20)               | 9 (26)           |
| Aeroallergy baseline, <i>n</i> (%)                                 | 2 (20)           | 2 (25)          | 3 (60)               | 13 (37)          |
| ICS baseline <sup>c</sup> , <i>n</i> (%)                           | 1 (10)           | 1 (13)          | 0                    | 4 (12)           |
| LABA baseline <sup>c</sup> , <i>n</i> (%)                          | 0                | 1 (13)          | 1 (20)               | 2 (6)            |
| LTRA baseline <sup>c</sup> , <i>n</i> (%)                          | 0                | 0               | 0                    | 1 (4)            |
| Exercise baseline, hours/week, median (Q1–Q3)                      | 12.5 (12.5–16.5) | 12.5 (8.5–12.5) | 12.5 (12.5–16.5)     | 12.5 (12.5–12.5) |
| Exercise change, baseline to follow-up, hours/week, median (Q1–Q3) | 0 (0–4)          | 0 (0–4)         | 0 (0–4)              | 0 (–4–4)         |

Abbreviations: 95% CI, 95% confidence interval; EIB, exercise-induced bronchoconstriction; FeNO, fractional exhaled nitric oxide; FEV<sub>1</sub>, forced expiratory volume in one second; FVC, forced vital capacity; ICS, inhaled corticosteroid; LABA, long-acting  $\beta_2$ -agonist; LTRA, leukotriene receptor antagonist; ppb, parts per billion; Q1, first quartile; Q3, third quartile; SD, standard deviation.

Note: Available data: All participants responded to all questions except ICS baseline *n* = 56, ICS follow-up *n* = 57, LABA baseline *n* = 54, LABA follow-up *n* = 56, and LTRA baseline *n* = 55.

<sup>a</sup>Reference value: Global Lung Initiative.

<sup>b</sup>Self-reported physician-diagnosed with symptoms and/or medication excluding single therapy with short-acting  $\beta_2$ -agonists.

<sup>c</sup>Any use in the preceding 3 months.

<sup>d</sup>*p* < 0.05 compared with EIB negative.

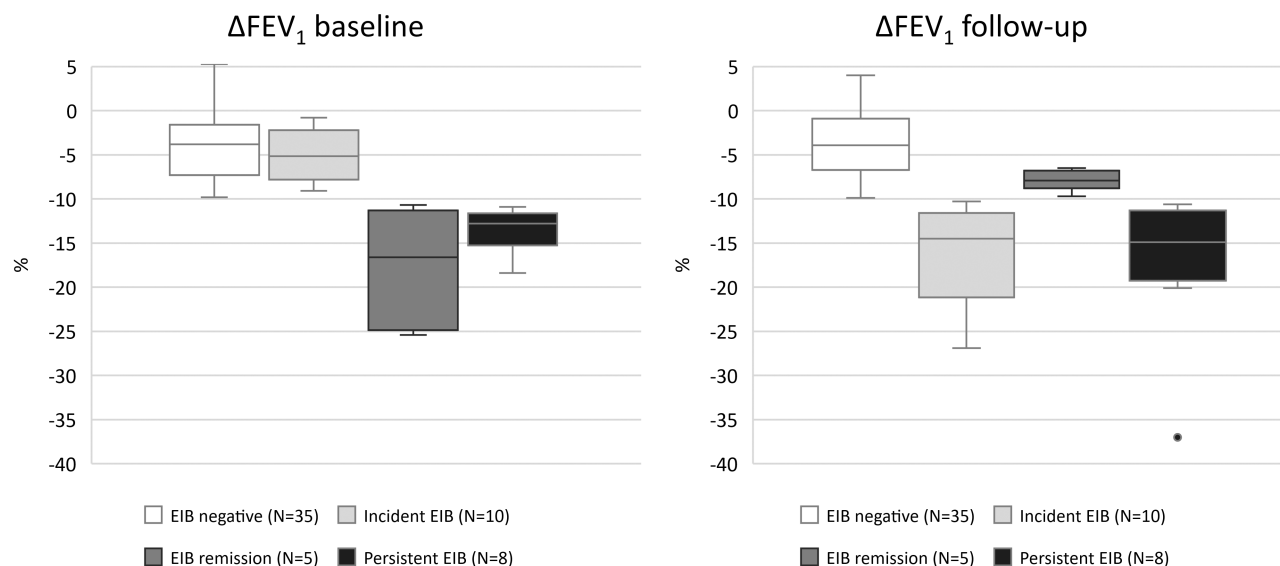
(22%) of the 45 participants who were EIB negative at baseline. Eight participants had persistent EIB, that is, 14% of the total study population. Reporting several asthma-like symptoms at baseline was associated with incident EIB at follow-up. No associations were found between exercise-induced respiratory symptoms, FeNO, or self-reported aeroallergy at baseline and incident EIB at follow-up. Incident EILO was found in 3 of 24 (12%) of this cohort. All five participants with EILO at follow-up were classified as having supraglottic EILO, those with persistent EILO were classified as supraglottic also at baseline.

To our knowledge, this is the first longitudinal study of EIB in high school athletes from multiple sports disciplines. Two ninths of participants who were EIB negative at baseline had incident EIB at follow-up, indicating that repeated assessments of airway response to hyperpnea over time may be important in young athletes. Previous prospective studies of EIB in athletes are scarce and no estimates of incidence are reported, but in a small study of adult triathletes, three out of seven developed EIB during a two-year follow-up period.<sup>17</sup> Stensrud et al. have demonstrated that cross-country skiers older than 25 years have a higher prevalence of

bronchial hyperresponsiveness than younger skiers<sup>12</sup> and Fitch et al. have shown that late-onset asthma is common among Olympians,<sup>25</sup> suggesting that the number of years of sports involvement may play a role in the development of respiratory pathology.

Reporting several asthma-like symptoms at baseline was associated with incident EIB at follow-up in the present study. Similar scores have been used to predict incident asthma in population-based studies.<sup>26</sup> A previous study reported wheeze to be associated with EIB in young athletes,<sup>27</sup> though in most studies of EIB in athletic populations, questions on respiratory symptoms have mainly focused on symptoms during or directly after exercise.<sup>4</sup>

Unlike reporting asthma-like symptoms, reporting exercise-induced respiratory symptoms at baseline was not related to incident EIB at follow-up. This is in line with previous cross-sectional studies in athletic populations, where respiratory symptoms during or in conjunction with exercise are reported to have poor predictive value for EIB.<sup>3,16</sup> However, in a study by Bougault et al., spontaneous reports of disabling exercise-induced respiratory symptoms from young soccer players to a physician during a clinical visit had some predictive value for EIB.<sup>28</sup>



**FIGURE 2** Change in FEV<sub>1</sub> from EIB tests at baseline and follow-up, displayed by results from EIB test at follow-up. Presented as median, Q1, Q3, and range. FEV<sub>1</sub>, forced expiratory volume in 1 s; EIB, exercise-induced bronchoconstriction; Q1, first quartile; Q3, third quartile.

**TABLE 2** Self-reported respiratory symptoms at baseline among participants who performed EIB test at follow-up, grouped by the result of EIB test at follow-up.

|  | Total<br>(n = 58) | Incident EIB<br>(n = 10) | Persistent EIB<br>(n = 8) | EIB remission<br>(n = 5) | EIB negative<br>(n = 35) |
|--|-------------------|--------------------------|---------------------------|--------------------------|--------------------------|
| Asthma-like symptoms <sup>a</sup>      |                   |                          |                           |                          |                          |
| 0 symptom, n (%)                       | 33 (57)           | 3 (30)                   | 5 (63)                    | 2 (40)                   | 23 (66)                  |
| 1 symptom, n (%)                       | 17 (29)           | 4 (40)                   | 1 (13)                    | 3 (60)                   | 9 (26)                   |
| ≥2 symptoms, n (%)                     | 8 (14)            | 3 (30)                   | 2 (25)                    | -                        | 3 (9)                    |
| Exercise-induced symptoms <sup>b</sup> |                   |                          |                           |                          |                          |
| 0 symptoms, n (%)                      | 13 (22)           | 3 (30)                   | 1 (13)                    | 1 (20)                   | 8 (23)                   |
| 1–2 symptoms, n (%)                    | 19 (33)           | 2 (20)                   | 3 (38)                    | 2 (40)                   | 12 (34)                  |
| 3–4 symptoms, n (%)                    | 10 (17)           | 2 (20)                   | 2 (25)                    | 1 (20)                   | 5 (14)                   |
| ≥5 symptoms, n (%)                     | 16 (28)           | 3 (30)                   | 2 (25)                    | 1 (20)                   | 10 (29)                  |

Note: No significant differences were detected between the groups.

<sup>a</sup>Wheeze, waking up with chest tightness, daytime shortness of breath, or waking up with shortness of breath. Any symptom in the preceding 12 months.

<sup>b</sup>Exercise-induced wheeze, chest tightness, shortness of breath, cough, throat tightness, choking sensation, hoarseness, or inspiratory noise. Any symptom more than once in the preceding 12 months.

Interestingly, in the same study the players' answers to questionnaires about exercise-induced symptoms were not predictive for EIB,<sup>28</sup> suggesting that symptom severity might matter, as it is likely that higher symptom burden would more often be spontaneously reported.

FeNO at baseline showed low predictive value for EIB development. This is in line with a previous cross-sectional study in athletes, where FeNO levels could not be used to distinguish between EIB-positive and EIB-negative individuals.<sup>29</sup> However, it is in contrast with studies of children and adolescents, where elevated FeNO has been associated with objective evidence of EIB.<sup>30</sup> This is probably partly due to different mechanisms underlying EIB

in some athletes and in the general population.<sup>31</sup> Recent studies have demonstrated different phenotypes of bronchial hyperresponsiveness and asthma in athletes with a large proportion of athletes having type 2 low inflammation<sup>32,33</sup> providing some explanation for the diverging results for FeNO and EIB between athlete populations and the general population.

No association was found regarding self-reported aeroallergy at baseline and incident EIB. This is in contrast to a study in swimmers and long-distance runners showing significant relations between allergy and bronchial hyperresponsiveness.<sup>34</sup> This may be explained by differences between objective and subjective aeroallergy

**TABLE 3** Logistic regression analyses of associations of asthma-like symptoms and exercise-induced symptoms at baseline and incident EIB at follow-up. EIB-negative  $n = 35$ , incident EIB  $n = 10$ .

|   | Participants, $n$ (%) | OR          | 95% CI             |
|---|-----------------------|-------------|--------------------|
| <i>Asthma-like symptoms</i>                               |                       |             |                    |
| Wheeze  | 12 (27)               | 2.25        | 0.50, 9.99         |
| Waking up with chest tightness                            | 11 (24)               | <b>4.83</b> | <b>1.06, 22.09</b> |
| Shortness of breath during daytime rest <sup>a</sup>      | 4 (9)                 | 13.36       | 0.92, 786.34       |
| Waking up with shortness of breath                        | 0                     | -           |                    |
| Numbers of asthma-like symptoms, continuous               |                       | <b>2.78</b> | <b>1.16, 6.58</b>  |
| <i>Asthma-like symptoms, categorical<sup>a</sup></i>      |                       |             |                    |
| 0 symptom (ref)   | 26 (58)               | 1.00        |                    |
| 1 symptom   | 13 (29)               | 3.29        | 0.46, 27.20        |
| ≥2 symptoms   | 6 (13)                | 6.99        | 0.65, 84.58        |
| <i>Exercise-induced symptoms</i>                          |                       |             |                    |
| Wheeze  | 16 (36)               | 1.28        | 0.31, 5.42         |
| Chest tightness   | 15 (33)               | 0.17        | 0.02, 1.47         |
| Shortness of breath                                       | 20 (46)               | 2.14        | 0.51, 9.02         |
| Cough   | 21 (47)               | 1.90        | 0.45, 7.98         |
| Throat tightness  | 20 (46)               | 1.67        | 0.38, 7.29         |
| Choking sensation <sup>a</sup>                            | 8 (18)                | 1.20        | 0.10, 8.66         |
| Hoarseness  | 13 (29)               | 2.31        | 0.51, 10.54        |
| Noise during inspiration                                  | 17 (38)               | 0.64        | 0.14, 2.92         |
| Numbers of exercise-induced symptoms, continuous          |                       | 1.03        | 0.79, 1.35         |
| <i>Exercise-induced symptoms, categorical<sup>a</sup></i> |                       |             |                    |
| 0 symptoms (ref)  | 11 (24)               | 1.00        |                    |
| 1–2 symptoms  | 14 (31)               | 0.46        | 0.03, 4.99         |
| 3–4 symptoms  | 7 (16)                | 1.06        | 0.07, 13.25        |
| ≥5 symptoms   | 13 (29)               | 0.80        | 0.08, 7.78         |

Abbreviations: 95% CI, 95% confidence interval; EIB, exercise-induced bronchoconstriction; OR, odds ratio.

Note: Confidence intervals not containing 1 are considered significant. Analyses made by logistic regression models or exact logistic regression models with each asthma-like symptom (exposure) and incident EIB (outcome), sum of asthma-like symptoms as a continuous variable (exposure) and incident EIB (outcome), and asthma-like symptoms as a categorical variable (exposure) and incident EIB. The same methods were used for exercise-induced symptoms and incident EIB.

<sup>a</sup>Analysis performed with exact logistic regression.

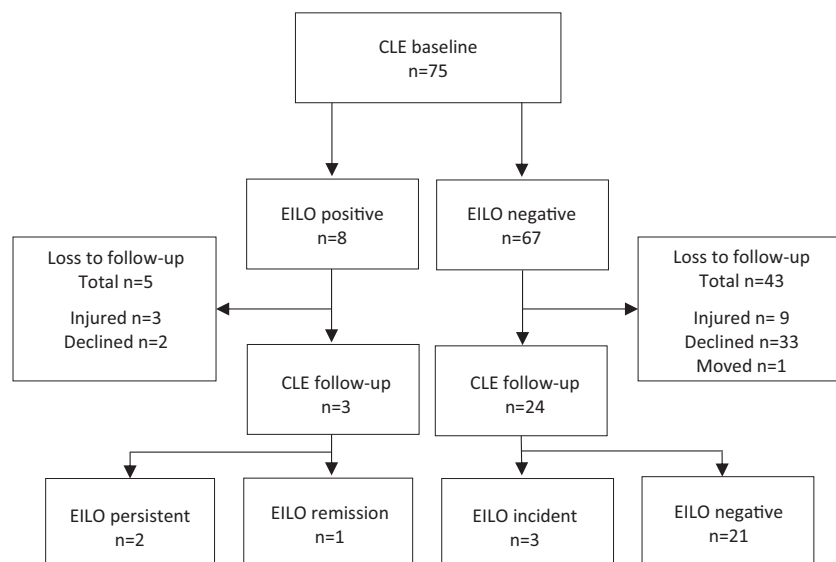
definitions as well as differences in the athletic environment: there were no swimmers in our population and a majority performed indoor sports.

Considering the large number of participants performing indoor sports, questions about aeroallergy to house dust mites, and molds could have rendered a more comprehensive variable for aeroallergy. Yet, sensitization to house dust mites or molds have been shown to be of limited prevalence among Swedish children and young adults compared with sensitization to furry animals or pollen.<sup>35</sup>

There was no association between sex and incident EIB in the present study. As previous prospective studies of

EIB are scarce, the effect of sex on the risk of developing EIB is unknown. In a meta-analysis by Rodriguez Bauza *et al* Silveyra, no sex difference was found regarding the prevalence of EIB in athletes. However, when accounting for atopic status, male athletes were more at risk of having EIB than female athletes.<sup>36</sup>

We found EILO in five out of 27 participants at follow-up, all classified as having supraglottic EILO. Two participants had persistent EILO, classified as supraglottic also at baseline. To date, there are no epidemiological studies of EILO over time—thus, incidence data are lacking. However, our results are in concordance with a



**FIGURE 3** Participation, loss to follow up, and results of CLE test during the study. CLE, continuous laryngoscopy exercise; EILO, exercise-induced laryngeal obstruction.

**TABLE 4** Results of CLE tests at baseline and follow-up.

|   | CLE test<br>baseline | CLE test<br>follow-up |
|---|----------------------|-----------------------|
| Participants, <i>n</i>                  | 75                   | 27                    |
| Female, <i>n</i> (%)                    | 49 (65)              | 19 (66)               |
| EILO, <i>n</i> (%)                      | 8 (11)               | 5 (19)                |
| Incident EILO, follow-up, <i>n</i>      | -                    | 3                     |
| Glottic, <i>n</i>                       | 2                    | 0                     |
| Supraglottic, <i>n</i>                  | 4                    | 5                     |
| Both glottic and supraglottic, <i>n</i> | 2                    | 0                     |

Abbreviations: CLE, continuous laryngoscopy exercise; EILO, exercise-induced laryngeal obstruction.

previous retrospective report, where supraglottic EILO seemed to remain over time in individuals who received conservative treatment.<sup>18</sup> In line with the present study, obstruction at the supraglottic level has been reported to be the dominating type of EILO in athletes.<sup>10</sup>

The strengths of this study include the longitudinal prospective approach with follow-up during sports high school, when many young athletes start pursuing an elite athlete career, the standardized EIB tests and CLE tests performed in accordance with current recommendations,<sup>11,24</sup> and the EIB tests being performed during the same time period (September–November) each year, limiting the impact of seasonal variability.<sup>34</sup>

A limitation of the study is the large loss to follow-up, possibly introducing a selection bias. However, no differences between subjects lost to follow-up and subjects included in the follow-up were found. Almost 38% of the participants who were lost to follow up for the EIB test had injuries preventing running on a treadmill. Price et al. have recommended caution when ruling on mild or borderline cases based on results from a single indirect

test for EIB in athletic individuals.<sup>37</sup> As most of the EIB-positive participants in the present study had mild EIB (a postexercise reduction in FEV<sub>1</sub> of 10%–25%), a second test could have rendered a more robust diagnosis. On the other hand, the standardized dry-air exercise test has good reproducibility, according to Anderson et al.<sup>38</sup>

The limited number of observations included in our regression models limited the possibility of performing adjustments and resulted in estimates with wide confidence intervals, suggesting a large uncertainty in our results.

## 4.1 | Perspective

It is important to facilitate high-achieving young athletes to be able to become successful senior athletes. The longitudinal approach of the present study provides novel insights into the course of EIB and EILO in young athletes attending sports high school. Screening young athletes for EIB has been suggested<sup>4,39</sup> but knowledge about how to select the athletes who would benefit most from such screening tests is limited. Our findings may support clinicians in their decision-making when selecting young athletes for objective testing for EIB.

Evaluating EILO is particularly important in young athletes<sup>11</sup> and our results might indicate that supraglottic EILO in young athletes persists over time. This highlights the need for clinical trials investigating treatment options for EILO in young athletes.

## 5 | CONCLUSION

Incident EIB and EILO are common in young athletes and repeated testing for EIB and EILO may be relevant in this group throughout their sports career. Questions



about asthma-like symptoms may be of value as part of a clinical algorithm supporting the selection of athletes to be referred for objective EIB testing.

## AUTHOR CONTRIBUTIONS

Karin Ersson: investigation (equal); data curation (lead); methodology (supporting); formal analysis (lead); writing—original draft preparation (lead); writing—reviewing and editing (equal). Elisabet Mallmin: investigation (equal); methodology (supporting); writing—reviewing and editing (equal). Leif Nordang: conceptualization (equal); investigation (equal); methodology (equal); writing—reviewing and editing (equal). Andrei Malinowski: conceptualization (equal); methodology (equal); formal analysis (supporting); writing—reviewing and editing (equal). Henrik Johansson: conceptualization (equal); methodology (equal); formal analysis (supporting); funding acquisition (lead); investigation (equal); writing—reviewing and editing (equal).

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## CONFLICT OF INTEREST STATEMENT

The authors have no conflict of interest to disclose.

## DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

## ORCID

Karin Ersson  <https://orcid.org/0000-0003-3185-3316>

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## SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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