

Original Article

Diagnosing Exercise-Induced Bronchoconstriction With Eucapnic Voluntary Hyperpnea: Is One Test Enough?

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What is already known about this topic? Indirect bronchoprovocation testing, specifically eucapnic voluntary hyperpnea (EVH), is currently recommended for the diagnosis of exercise-induced bronchoconstriction (EIB). However, the clinical reproducibility of this methodology has yet to be appropriately established, presenting a potential for misdiagnosis.

What does this article add to our knowledge? This article highlights the need for caution when making a diagnosis of EIB on the basis of a solitary EVH assessment to reduce the potential for misdiagnosis. Indeed, when encountering patients with a mild or borderline reduction in lung function postchallenge, we recommend that more than one EVH test is performed to exclude or confirm a diagnosis of EIB.

How does this study impact current management guidelines? The application of treatment for EIB in athletes should be initiated only when a diagnosis has been correctly established.

BACKGROUND: In athletic individuals, a secure diagnosis of exercise-induced bronchoconstriction (EIB) is dependent on objective testing. Indirect bronchoprovocation testing is often used in this context and eucapnic voluntary hyperpnea (EVH) testing is recommended for this purpose, yet the short-term reproducibility of EVH is yet to be appropriately established. **OBJECTIVE:** The aim of this study was to evaluate the reproducibility of EVH in a cohort of recreational athletes. **METHODS:** A cohort of recreational athletes ($n = 32$) attended the laboratory on two occasions to complete an EVH challenge, separated by a period of 14 or 21 days. Spirometry and impulse oscillometry was performed before and after EVH. Training load was maintained between visits. **RESULTS:** Prechallenge lung function was similar at both visits ($P > .05$). No significant difference was observed in maximum change in FEV₁ (Δ FEV_{1max}) after EVH between visits ($P > .05$), and test-retest Δ FEV_{1max} was correlated (intraclass correlation coefficient = 0.81; $r^2 = 0.66$; $P = .001$). Poor diagnostic reliability was observed between tests; 11 athletes were diagnosed with EIB (on the basis of Δ FEV_{1max} $\geq 10\%$) at visit 1 and at visit 2. However, only 7 athletes were positive at both visits. Although

there was a small mean difference in Δ FEV_{1max} between tests (-0.6%), there were wide limits of agreement (-10.7% to 9.5%). Likewise, similar results were observed for impulse oscillometry between visits.

CONCLUSIONS: In a cohort of recreational athletes, EVH demonstrated poor clinical reproducibility for the diagnosis of EIB. These findings highlight a need for caution when confirming or refuting EIB on the basis of a single indirect bronchoprovocation challenge. When encountering patients with mild or borderline EIB, we recommend that more than one EVH test is performed to exclude or confirm a diagnosis. © 2014 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2014;■:■-■)

Key words: Airway dysfunction; Athletes; Eucapnic voluntary hyperpnea; Exercise-induced bronchoconstriction; Indirect bronchoprovocation testing; Reproducibility

Exercise-induced bronchoconstriction (EIB) describes the transient airway narrowing that occurs in association with exercise. It is prevalent in both elite and recreational athletes¹ and may impact upon both their respiratory health and athletic performance.²⁻⁴ It is now well established that the diagnosis of EIB in athletes should not be based on clinical assessment alone⁵⁻⁷ since a poor correlation exists between exercise-associated respiratory symptoms and objective evidence of airway narrowing.⁸ As a consequence of this dissociation, current guidelines recommend that objective bronchoprovocation testing should be employed to secure a diagnosis of EIB.^{9,10}

Exercise testing is frequently employed to diagnose EIB. Although an exercise test is ecologically valid and possesses good specificity for diagnosis, it has poor sensitivity and is limited by difficulties in controlling environmental conditions and exercise load and thus, the airway stimulus during a challenge.¹¹ Indeed, poor short-term reproducibility of a laboratory exercise test for the diagnosis of EIB in a nonathletic group has previously been observed, with the conclusion that one test may not be enough to

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*Abbreviations used**AQUA- Allergy Questionnaire for Athletes**AUC- Area under the curve**EIB- Exercise-induced bronchoconstriction**EVH- Eucapnic voluntary hyperpnea**ICC- Intraclass correlation coefficient**IOS- Impulse oscillometry**LOA- Limit of agreement*

secure a diagnosis.¹² Several “indirect” airway challenges have been developed and recommended as surrogate means for diagnosing EIB. The International Olympic Committee-Medical Commission¹³ and several other guideline committees strongly endorse the eucapnic voluntary hyperpnea (EVH) challenge in this capacity.^{9,10} The EVH challenge uses a compressed, dry gas as the stimulus for provoking bronchoconstriction with controlled hyperpnea.

The EVH test has been used and recommended for screening athletic cohorts for EIB,^{14,15} with a positive “diagnosis” being made from a single provocation test. However, there is sparse data regarding the reproducibility of EVH,^{16,17} and the inherent variability in any test has pragmatic implications for evaluating the effectiveness of a diagnostic tool in screening programs and interventions. Moreover, the reliability of EVH testing in the population of athletes in whom EVH screening has been advocated (ie, team squads^{15,18} at amateur or varsity level) has not been established. In this population, the fall in FEV₁ postchallenge can often be borderline (ie, 10%-15% fall) and thus it is important to determine the stability and thus the precision of such a result.

We therefore undertook this study with the aim of evaluating the test-retest reproducibility of EVH in a cohort of recreational athletes. We proposed that there would be no difference in airway response after EVH between visits; that is, EVH would have good test-retest reproducibility. A secondary aim was to evaluate the reproducibility of measures of small airway function using impulse oscillometry (IOS) over the same period of time.

METHODS

Study population

Thirty-six recreational athletes (training 6 ± 1 h/wk; men: $n = 31$) from various sporting disciplines—endurance ($n = 22$; runners, cyclists, and triathletes), intermittent high-intensity ($n = 11$; soccer, rugby, and hockey), and nonendurance ($n = 3$; weightlifters)—were recruited to take part in the study. All subjects were nonsmokers, free from respiratory, cardiovascular, metabolic, and psychiatric disease, and any other significant medical condition except mild asthma. Six subjects had a physician-based diagnosis of mild asthma; all were prescribed a short-acting beta-2 agonist, and two were prescribed a regular inhaled corticosteroid.

Experimental design

All subjects were required to attend the laboratory on two occasions separated by a period of either 14 or 21 days. Subjects entered the laboratory 1-hour postprandial at a similar (± 1 hour) time of day for each visit. An assessment of respiratory health and evaluation of allergy status was determined via completion of the Allergy Questionnaire for Athletes (AQUA) and aeroallergen skin prick testing. Spirometry and IOS maneuvers were performed before and after an EVH provocation challenge.

Subjects were instructed to maintain their normal diet and physical activity levels throughout the duration of the study, and compliance with this regime was assessed by interview. Exclusion occurred if any alteration in training and/or health status/allergen exposure or respiratory tract infection was reported. Subjects were asked to abstain from strenuous physical activity and short-acting beta-2 agonist medication for 24 hours and inhaled corticosteroid for 72 hours, respectively, before each laboratory visit. All tests and procedures were approved by the local research ethics committee, and all subjects provided written informed consent for experimentation with human subjects.

Atopic status

Sensitivity to seven common airborne allergens (early blossom tree, mid blossom tree, grass, weed, mould, cat, and dust mite) was assessed via skin prick testing.¹⁹ Subjects also completed AQUA to assess allergic symptoms.²⁰ An athlete was considered to be allergic if they presented with a positive skin prick test result and a positive AQUA score (≥ 5).

Pulmonary function

Spirometry. Lung function was assessed by using forced flow-volume spirometry (MicroLoop ML3535; Cardinal Health, UK).²¹ Subjects with airway obstruction at visit 1 (FEV₁/forced vital capacity, <0.7 ; FEV₁ % predicted, <0.8) were excluded.

Eucapnic voluntary hyperpnea. A modified version of the EVH was performed on the basis of the protocol described previously.^{17,22} Briefly, subjects breathed a dry compressed gas mixture (21% O₂, 5% CO₂, balance N₂) at a target ventilation rate equivalent to 85% (baseline FEV₁ $\times 30$) of their predicted maximal voluntary ventilation for 6 minutes. Subjects received real-time visual feedback of their ventilation to ensure that they maintained the target level. Spirometry was performed in triplicate at baseline and in duplicate at 3, 5, 7, 10, and 15 minutes after EVH. Values within 5% were considered acceptable.²¹ The highest recorded value at each time point was used for analysis. A positive diagnosis for EIB was defined by a fall of 10% or more in FEV₁ at two consecutive time points after the EVH challenge in accordance with International Olympic Committee-Medical Commission recommendations.¹³ The severity of EIB was classified according to the magnitude of reduction in FEV₁: mild ($\geq 10\%$ - $<25\%$), moderate ($\geq 25\%$ - $<50\%$), or severe ($\geq 50\%$).

IOS technique. IOS measures were obtained (MasterLab IOS System; Erich Jaeger Co, Wurzburg, Germany) in accordance with international recommendations,²³ prior to spirometry, immediately before and after EVH. In brief, subjects performed 30 seconds of tidal breathing before a maximal inspiratory maneuver followed by a passive expiratory maneuver.

Statistical analysis

It was calculated that a sample size of 32 subjects would provide statistical power above 80%, with an alpha level of 0.05. Normally distributed data are expressed as mean $\pm$ SD or 95% CIs. Significance was set at $P < .05$. A two-sided paired t test was used to evaluate differences in variables between visits. Pearson intraclass correlation coefficient (ICC) was calculated using a two-way mixed effect model with the mean single measure reported; ICC ranges from -1 to $+1$, with the latter indicating perfect agreement. Reproducibility was assessed using the method described by Bland and Altman,²⁴ with difference

TABLE I. Subjects' (n = 32) clinical characteristics

Variable	Value
Sex (M:F)	28:4
Age (y)	28 ± 7
Height (cm)	178.3 ± 6.5
Weight (kg)	81.4 ± 12.0
BMI (kg/m ²)	25.6 ± 3.3
Training (h/wk)	6 ± 1
Physician-diagnosed asthma	6 of 32 (19%)
Self-report symptoms	10 of 32 (31%)
AQUA ⁺	18 of 32 (56%)
Atopic	18 of 32 (56%)

BMI, Body mass index; F, female; M, male.

Data presented as mean ± SD

TABLE II. Baseline pulmonary function

Baseline pulmonary function	Visit 1	Visit 2
FEV ₁ (L)	4.45 ± 0.75	4.40 ± 0.76
FEV ₁ (% predicted)	101.5 ± 11.8	100.3 ± 12.6
FVC (L)	5.51 ± 0.83	5.56 ± 0.75
FVC (% predicted)	105.6 ± 11.9	106.8 ± 10.9
FEV ₁ /FVC (%)	80.9 ± 6.0	78.99 ± 7.37*
R ₅ (kPa/(L · s))	0.29 ± 0.09	0.27 ± 0.06
R ₂₀ (kPa/(L · s))	0.25 ± 0.06	0.24 ± 0.05
X ₅ (kPa/(L · s))	−0.10 ± 0.10	−0.08 ± 0.02
Z ₅ (kPa/(L · s))	0.30 ± 0.09	0.29 ± 0.06
R _F (Hz)	11.69 ± 4.44	11.68 ± 3.55
A _x (Hz.kPa/(L · s))	0.32 ± 0.44	0.25 ± 0.17

A_x, Area of reactance (area integrated from 5 Hz to R_F); FVC, forced vital capacity; R_F, resonance frequency; R₅, resistance at 5 Hz; R₂₀, resistance at 20 Hz; X₅, reactance at 5 Hz; Z₅, magnitude of impedance at 5 Hz.

Data presented as mean ± SD, n = 32.

*Different from visit 1 ($P < .01$).

expressed as mean bias (ie, mean difference between group measures) and upper and lower 95% limits of agreement (LOAs). Area under the curve (AUC)_{0-15min} was calculated by using the trapezoidal method and expressed as percentage fall in FEV₁. Data were analyzed using PASW Statistics 19 statistical software package (SPSS, Inc, version 19, Chicago, Ill) and GraphPad Prism (version 5.0; GraphPad Software, San Diego, Calif).

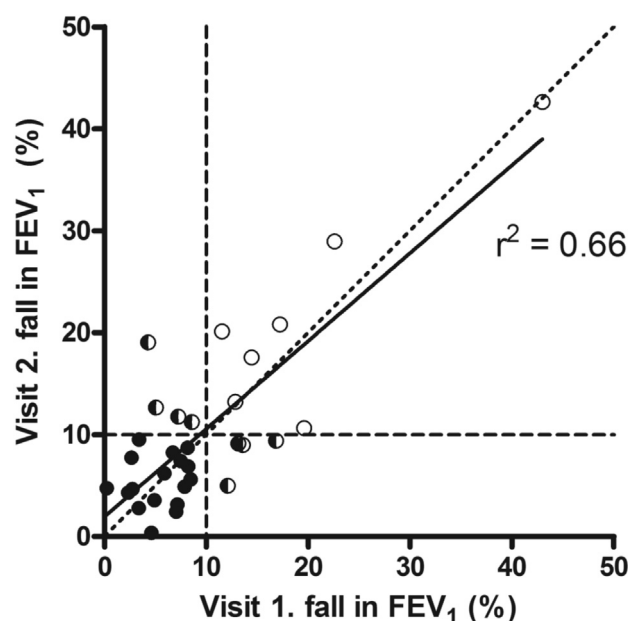
RESULTS

Thirty-two athletes (men: n = 28) completed the study. One athlete was excluded at the initial visit on the basis of resting airway obstruction, and three athletes were excluded because of illness. Subjects' characteristics are presented in Table I.

Baseline characteristics and prechallenge lung function

Eighteen athletes (56%) were atopic to skin prick tests, and 18 (56%) had a positive (≥ 5) AQUA score. Thirteen athletes (41%) with a positive AQUA score were also atopic and therefore considered allergic. Exercise-associated respiratory symptoms (eg, cough, wheeze, and dyspnea) were reported by 10 (31%) athletes.

At baseline, all pulmonary function measures were within normal predicted limits, with no evidence of airflow obstruction (Table II). Resting spirometric variables were similar between

**FIGURE 1.** Relationship between fall in FEV₁ after EVH between visits. Closed circles indicate negative athletes, open circles indicate positive athletes at both visits, and split circles indicate positive athletes at one visit. Broken horizontal and vertical lines indicate the diagnostic threshold.

visits except for FEV₁/forced vital capacity ($P < .01$). All IOS measures were similar between visits.

Short-term reproducibility (n = 32)

Similar ventilation rates were achieved at both visits (visit 1, 113 ± 25 L/min; visit 2, 119 ± 25 L/min; $P = .08$). Target ventilation was achieved at visit 1 (84.6%) and visit 2 (90.4%). Eleven athletes (34% of the cohort) were diagnosed with EIB at visit 1 (mild, n = 10; moderate, n = 1) and 11 athletes at visit 2 (mild, n = 9; moderate, n = 2). Seven athletes were positive at visit 1 and visit 2 (endurance athletes, n = 5; intermittent high-intensity athletes, n = 1; nonendurance athletes, n = 1). Seventeen subjects (75%) were negative on both occasions.

In those with a previous physician diagnosis of asthma (n = 6), 4 (66%) were positive at visit 1 (mild, n = 3; moderate, n = 1) and 3 (50%) at visit 2 (mild, n = 2; moderate, n = 1). Two were positive on both occasions (mild, n = 1; moderate, n = 1). A diagnosis of asthma, therefore, provided a positive and negative predictive value of 33% and 94%, respectively, for the diagnosis of EIB at either visit.

Eight athletes with allergy (25%) were positive at visit 1, and 6 (19%) were positive at visit 2. Four athletes with allergy (13%) were positive on both occasions. Allergy, therefore, provided a positive and negative predictive value of 67% and 82% respectively, for the diagnosis of EIB at either visit.

No difference was observed in maximum change in FEV₁ (Δ FEV_{1max}) after EVH between visits (visit 1, −9.8%; visit 2, −10.4%; $P = .51$; 95% CI, 6.5–7.8) and test-retest Δ FEV_{1max} was correlated (ICC = 0.81; $r^2 = 0.66$; $P = .001$) (Figure 1). Although there was only a small bias in Δ FEV_{1max} between tests (−0.6%), the data exhibited wide LOAs (−10.7% to 9.5%) (Figure 2). In addition, no difference was observed for

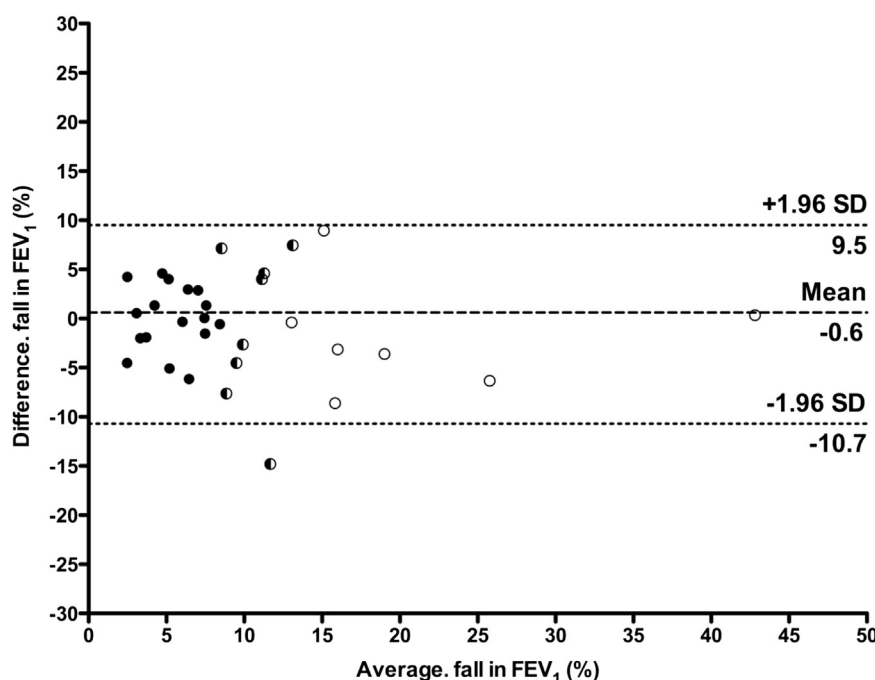


FIGURE 2. Bland-Altman plot of the maximum reduction in FEV₁ after EVH between visits. *Closed circles* indicate negative athletes, *open circles* indicate positive athletes at both visits, and *split circles* indicate positive athletes at one visit.

AUC_{0-15min} % fall in FEV₁ between visit 1 (98.3%) and visit 2 (107.0%) ($P = .33$) (Figure 3) and test-retest was correlated ($ICC = 0.85$; $r^2 = 0.73$; $P = .001$). No difference was observed for resting %FEV₁ predicted between the day of the positive test ($98.7\% \pm 12.2\%$) and the day of the negative test ($98.8\% \pm 14.0\%$) ($P = .97$). In addition, no difference was observed when both tests were either negative ($P = .66$) or positive ($P = .16$).

Nonasthmatic athletes (n = 26)

When excluding athletes with mild asthma from the analysis (n = 6), no difference was observed in maximum change in FEV₁ (ΔFEV_{1max}) after EVH between visits (visit 1, -8.2% ; visit 2, -9.0% ; $P = .41$; 95% CI, 6.3-8.0) and test-retest ΔFEV_{1max} was correlated ($ICC = 0.66$; $r^2 = 0.43$; $P = .001$). Although there was only a small bias in ΔFEV_{1max} between tests (-0.9%), the data exhibited wide LOAs (-11.0% to 9.3%). In addition, no difference was observed for AUC_{0-15min} % fall in FEV₁ between visit 1 (78.2%) and visit 2 (88.5%) ($P = .29$) and test-retest was correlated ($ICC = 0.73$; $r^2 = 0.53$; $P = .001$).

Impulse oscillometry (n = 32)

No difference was observed in any of the IOS variables after EVH between visits ($P > .05$) (Table III). Although significant correlations were observed between visits for resistance at 5 Hz ($ICC = 0.89$; $r^2 = 0.80$), resistance at 20 Hz ($ICC = 0.80$; $r^2 = 0.64$), reactance at 5 Hz ($ICC = 0.62$; $r^2 = 0.39$), magnitude of impedance at 5 Hz ($ICC = 0.89$; $r^2 = 0.80$), resonance frequency ($ICC = 0.94$; $r^2 = 0.89$), and area of reactance (area integrated from 5 Hz to resonance frequency) ($ICC = 0.94$; $r^2 = 0.87$) ($P = .001$), all variables exhibited wide LOAs.

DISCUSSION

In a cohort of recreational athletes, EVH demonstrates poor diagnostic test-retest reproducibility over a short-term period of assessment. This finding has implications for the clinical utility and application of EVH as a bronchoprovocation challenge in the diagnosis of EIB, specifically when it is used in a population of recreational athletes with mild reductions in lung function after a challenge. Moreover, it highlights the need for caution when EVH is used as a screening tool for EIB in a comparable population.

Reproducibility is important in characterizing the diagnostic utility of a test. A high level of short-term, clinically relevant, test-retest reproducibility is vital for clinicians to adopt a diagnostic procedure. This is particularly pertinent in the context of EIB where the differential diagnosis for exercise-associated dyspnea is broad²⁵ and several conditions mimic transient airflow narrowing, for example, exercise-induced laryngeal obstruction.²⁶ The implications of over- and underdiagnosis of EIB in elite athletes have previously been raised.⁶ For example, a false-positive/false-negative diagnosis has implications on health (eg, unnecessary medication) and performance (eg, reduced ability), respectively.

Our findings indicate that although there was a good correlation in the change in FEV₁ (ie, fall in lung function) between visits, a Bland-Altman plot, which is a clinically relevant assessment of reproducibility,²⁴ revealed wide LOAs. Specifically, in the present study, 15 athletes (47%) were diagnosed with EIB at either visit 1 ($\Delta FEV_{1, -17.9\% \pm 9.0\%}$) or visit 2 ($\Delta FEV_{1, -19.0\% \pm 9.6\%}$) but only seven athletes (22%) were diagnosed positive at both visits. This was despite strict regulation of training and environmental conditions between visits and similar ventilation during the challenge. Therefore, when

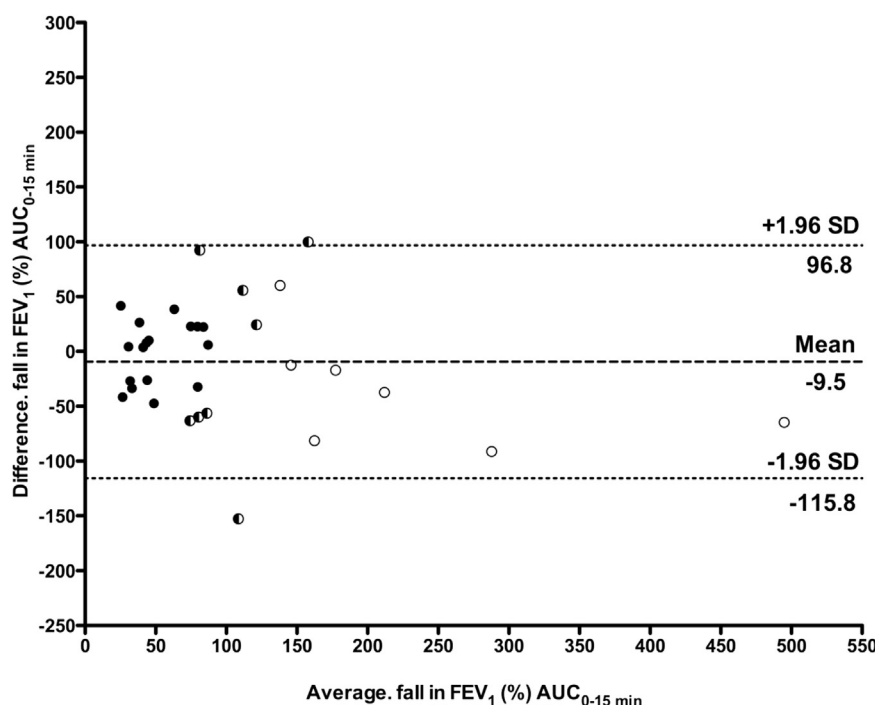


FIGURE 3. Bland-Altman plot of the $AUC_{0-15\text{min}}$ after EVH between visits. *Closed circles* indicate negative athletes, *open circles* indicate positive athletes at both visits, and *split circles* indicate positive athletes at one visit.

TABLE III. IOS variables after EVH between visits

IOS variable	Visit 1	Visit 2
R_5 (kPa/(L · s))	0.36 ± 0.11	0.37 ± 0.13
R_{20} (kPa/(L · s))	0.29 ± 0.10	0.27 ± 0.07
X_5 (kPa/(L · s))	-0.11 ± 0.07	-0.13 ± 0.08
Z_5 (kPa/(L · s))	0.38 ± 0.12	0.38 ± 0.15
R_F (Hz)	16.15 ± 5.95	16.02 ± 5.98
A_x (Hz.kPa/(L · s))	0.73 ± 0.87	0.78 ± 1.04

A_x , Area of reactance (area integrated from 5 Hz to R_F); R_F , resonance frequency; R_5 , resistance at 5 Hz; R_{20} , resistance at 20 Hz; X_5 , reactance at 5 Hz; Z_5 , magnitude of impedance at 5 Hz.

Data presented as mean $\pm$ SD, $n = 32$.

applying a threshold of 10% or more fall in FEV_1 for the diagnosis of EIB,²⁷ the inherent variability in the test between visits raises significant clinical diagnostic implications, particularly in athletes presenting with mild EIB. Indeed, in the small number of athletes ($n = 4$) with a fall of 20% or more in FEV_1 , their EVH test result remained positive at both visits.

Variability in bronchial responsiveness has been previously observed with direct bronchoprovocation challenges.²⁸⁻³⁰ However, because airway hyperresponsiveness to pharmacologic agents such as methacholine differs from hyperresponsiveness to exercise or osmotic agents³¹ and does not infer the presence of inflammatory cells or mediators,³² indirect bronchoprovocation challenges such as exercise or surrogate challenges are more appropriate for the diagnosis of EIB.³³

Previous research evaluating EVH indicates good reproducibility in the maximum fall in FEV_1 after the challenge.^{16,17} Argyros et al¹⁷ observed no difference in the degree of bronchoconstriction over a 6-week period after EVH. However, the

magnitude of the fall in FEV_1 ($-27\% \pm 11\%$) was much greater than that in the present study ($-10\% \pm 8\%$) and they did not calculate LOAs. Stadelmann et al¹⁶ demonstrated similar findings, with LOAs at 6% for ΔFEV_1 between challenges. Although the average reduction in FEV_1 was equivalent to that in the present study, the time interval between tests was highly variable and evidence of training load maintenance was not reported. Furthermore, because the population consisted of highly competitive swimmers, a unique pathophysiological basis to the development of EIB (ie, airway injury)³⁴ may be apparent and thus differ from the population of the present study. Good reproducibility has previously been established for indirect tests such as the dry powder mannitol challenge in asthmatic children,³⁵ but this again has not been evaluated in a recreationally athletic cohort.

In keeping with our findings, recent evidence has highlighted the potential diagnostic pitfalls of performing a one-off exercise test for the diagnosis of EIB in subjects with possible asthma symptoms. Anderson et al¹² found that 89 of 373 (24%) individuals tested positive after an exercise challenge (based on a $\geq 10\%$ fall in FEV_1) at one of two visits. Similar findings were apparent in a study of asthmatic patients “screened” using a dry gas exercise test with a diagnostic cutoff of 15% fall in FEV_1 .³⁶ The authors concluded that more than one test may be required to exclude or confirm EIB.¹² The findings from the present study suggest this recommendation with EVH testing.

The reason for the poor reproducibility is not clear; however, environmental factors and/or physiological variation have a significant impact on variability.³⁷ Airway caliber fluctuates throughout the day and over short-term periods.³⁸ Airway hyperresponsiveness in elite swimmers assessed by EVH and methacholine has previously been shown to reduce over a short-term period as a result of a reduction in training load.³⁴

In the present study, no difference was observed in baseline FEV₁ and ventilation achieved during EVH remained unchanged between visits. Moreover, in those athletes who tested positive on only one occasion, no difference was observed in FEV₁ on the day of the positive test versus the day of the negative test.

A secondary aim of this study was to evaluate the stability of small airway function determined by IOS. The latter provides an alternative method for measuring and monitoring lung function and is advantageous in that the test is noneffort dependent and potentially evaluates small airway function. The technique has previously been found to be an acceptable measure to supplement spirometry after EVH.³⁹⁻⁴¹ The present study indicates that IOS variables appear to exhibit a similar degree of variability to spirometry after EVH, and as such does not support the notion of superiority when used to assess airway caliber in this setting.

Methodological considerations/future research

The present study focused on assessing the utility of EVH in a population of individuals with few symptoms, as per AQUA assessment. Moreover, the fall in FEV₁ posttest was mild, with few subjects demonstrating moderate or severe degrees of bronchoconstriction. For example, when athletes were positive at only one visit, an average fall in FEV₁ of 10.5% (range, 4.9%-19.1%) was observed (ie, mild). The population of positive individuals could therefore be viewed as "borderline" positive for a diagnosis of EIB. Accordingly, the findings of the present study are applicable specifically to individuals presenting a mild severity (ie, $\geq 10\%$ - $<25\%$ fall in FEV₁) reduction in lung function. This population is clinically relevant and is frequently reported in screening studies^{6,18,42,43} but by the nature of the cutoff values is often classified as borderline positive.

The optimum diagnostic "cutoff" for a diagnosis of EIB is not clear. The current value of 10% or more has been recommended since early use of the test and translated from both asthmatic and nonasthmatic populations.^{17,22,44} In the present study, the mean fall in negative athletes after EVH was $5.7\% \pm 2.5\%$ and thus comparable with previous literature.¹⁵ In contrast to the proposed bronchodilatory response observed after exercise,⁴⁵ the "normal" population mean response to EVH appears to be bronchoconstriction. Indeed, the provocative stimulus to the airways during EVH is highly potent and further work is needed to determine an appropriate cutoff specifically in endurance athletes who generally achieve high ventilation rates.

CONCLUSIONS

EVH is currently recommended as a key bronchoprovocation challenge for the diagnosis of EIB in athletes. This study demonstrates poor diagnostic reproducibility over a short-term period of assessment in recreational athletes, when a cutoff value of 10% or more fall in FEV₁ is employed. Accordingly, the findings indicate the need for caution when clinicians make a diagnosis on the basis of a solitary EVH assessment and suggest that further assessment and/or surveillance be considered. Therefore, when encountering patients with a mild or borderline reduction in lung function postchallenge, we recommend that more than one EVH test be performed to exclude or confirm a diagnosis. This is important to minimize the chance of misdiagnosis and thus mistreatment.

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