BMJ Open Sport & Exercise Medicine

Unsupervised field-based exercise challenge tests to support the detection of exercise-induced lower airway dysfunction in athletes

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To cite: Reier-Nilsen T, Stang JS, Flatsetøy H, *et al*. Unsupervised field-based exercise challenge tests to support the detection of exercise-induced lower airway dysfunction in athletes. *BMJ Open Sport & Exercise Medicine* 2023;**9**:e001680. doi:10.1136/bmjsem-2023-001680

Accepted 9 July 2023

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ABSTRACT

Background Athletes are at risk for developing exercise-induced lower airway narrowing. The diagnostic assessment of such lower airway dysfunction (LAD) requires an objective bronchial provocation test (BPT).

Objectives Our primary aim was to assess if unsupervised field-based exercise challenge tests (ECTs) could confirm LAD by using app-based spirometry. We also aimed to evaluate the diagnostic test performance of field-based and sport-specific ECTs, compared with established eucapnic voluntary hyperpnoea (EVH) and methacholine BPT.

Methods In athletes with LAD symptoms, sensitivity and specificity analyses were performed to compare outcomes of (1) standardised field-based 8 min ECT at 85% maximal heart rate with forced expiratory volume in 1 s (FEV_1) measured prechallenge and 1 min, 3 min, 5 min, 10 min, 15 min and 30 min postchallenge, (2) unstandardised field-based sport-specific ECT with FEV_1 measured prechallenge and within 10 min postchallenge, (3) EVH and (4) methacholine BPT.

Results Of 60 athletes (median age 17.5; range 16–28 years.; 40% females), 67% performed winter-sports, 43% reported asthma diagnosis. At least one positive BPT was observed in 68% (n=41/60), with rates of 51% (n=21/41) for standardised ECT, 49% (n=20/41) for unstandardised ECT, 32% (n=13/41) for EVH and methacholine BPT, while both standardised and unstandardised ECTs were simultaneously positive in only 20% (n=7/35). Standardised and unstandardised ECTs confirmed LAD with 54% sensitivity and 70% specificity, and 46% sensitivity and 68% specificity, respectively, using EVH as a reference, while EVH and methacholine BPT were both 33% sensitive and 85% specific, using standardised ECTs as reference.

Conclusion App-based spirometry for unsupervised field-based ECTs may support the diagnostic process in athletes with LAD symptoms.

Trial registration number NCT04275648.

WHAT IS ALREADY KNOWN ON THIS TOPIC?

⇒ Exercise-induced lower airway narrowing may result in lower airway dysfunction (LAD), a highly prevalent condition in endurance athletes, particularly in winter and pool-based sports.
⇒ The lack of association between clinical symptoms of LAD and detection of exercise-induced lower airway narrowing in athletes requires an objective bronchial provocation test (BPT) to confirm the diagnosis of LAD.
⇒ An exercise challenge test (ECT) would presumably be the best way to detect exercise-induced lower airway narrowing and confirm the LAD diagnosis. Still, ECTs are resource-demanding and challenging to standardise.
⇒ Laboratory tests, including the eucapnic voluntary hyperpnea (EVH) and the methacholine BPT, are widely used as surrogates to ECTs to document LAD in athletes.

WHAT THIS STUDY ADDS

⇒ Using app-based spirometry for unsupervised field-based ECTs may detect lower airway narrowing in more athletes than EVH and methacholine BPT.
⇒ In athletes with symptoms suggestive of LAD, unsupervised field-based ECTs using app-based spirometry may facilitate the diagnostic process.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE AND/OR POLICY

⇒ App-based spirometry may aid the diagnostic process of athletes with LAD symptoms.
⇒ The app-based spirometry is easily available and has low cost, which may reduce the worldwide gap in access to appropriate assessment of athletes with LAD symptoms.

INTRODUCTION

Athletes are at risk for developing exercise-induced lower airway narrowing.[1 2] This condition is mainly caused by a release of local inflammatory mediators (eg, prostaglandins, leukotrienes, histamine) in response to evaporative water-loss from the airway surface[3 4] and may be exacerbated by dry or cold air,[5] or inhaling allergens.[3] Symptoms suggestive of exercise-induced lower airway narrowing are

excessive mucus, wheezing, cough, chest tightness and dyspnoea.[6] Several clinical definitions have been used interchangeably for this condition, for example, exercise-induced asthma, exercise-induced bronchoconstriction and airway hyper-responsiveness, prompting the need for the recently introduced collective term, lower airway dysfunction (LAD).[2 7]

A correct diagnosis of LAD is important to normalise lung function and enable exercise without symptoms.[8] In athletes, symptoms of LAD are poorly associated with detecting lower airway narrowing by an objective bronchial provocation test (BPT) to confirm the diagnosis.[9–11] Thus, the International Olympic Committee-Medical Commission (IOC)[8] and the World Anti-Doping Agency[12] refer to Global Initiative for Asthma[13] and strongly suggest the presence of both LAD symptoms and a positive BPT before appropriate LAD therapy is initiated in this group. Presumably, the best way to detect exercise-induced lower airway narrowing would be to assess lung function before and after a relevant training session, that is, an exercise challenge test (ECT).[14] However, ECTs are resource-demanding in healthcare personnel and equipment, and challenging to standardise in terms of ambient conditions, exercise duration and workload.[15 16] Therefore, laboratory BPTs are often used as surrogate diagnostic tests for ECT. Direct BPTs stimulate bronchial smooth muscle contraction to provoke airway narrowing, most commonly by inhalation of methacholine.[4 17] In indirect BPTs, airway narrowing is induced by mimicking the pathophysiology of exercise through eucapnic voluntary hyperpnoea (EVH), or by inhaling strategies using mannitol or nebulised adenosine 5′-monophosphate. Based on its high specificity in confirming LAD, EVH has been suggested as the 'gold standard' for diagnosing LAD in athletes.[8 13] However, a recent systematic review from an IOC consensus group[14] showed that if ECTs are field based and sport specific, they seemed to have similar specificity and somewhat higher sensitivity than EVH to confirm LAD.

In the present paper, the objective was to assess if the novel concept of including a wireless, hand-held turbine-spirometer connected to a cloud-based smartphone application for unsupervised field ECTs, could aid the diagnostic process in athletes with LAD symptoms. First, we aimed to assess if unsupervised field-based ECTs could confirm LAD using app-based spirometry. Second, we aimed to evaluate the diagnostic test performance of field-based ECTs compared with EVH and methacholine BPT.

METHODS

Study design

In this open diagnostic study examining athletes with LAD symptoms, all participants went through, in random order, at least one standardised field-based ECT, at least one unstandardised field-based sport-specific ECT, an EVH and a methacholine BPT, on four different days within 4 weeks (figure 1). In the last 6 hours before BPTs, participants were instructed to avoid strenuous exercise, heavy meals, caffeine-containing food or beverage, and nicotine. Any use of beta2-agonists, ipratropiumbromide or other asthma medication was discontinued before all BPTs, in line with the European Respiratory Society (ERS) guidelines.[18]

Study population

Athletes aged 16–50 years, with LAD symptoms (ie, excessive mucus, wheezing, cough, chest tightness, dyspnoea) for >3 months and with current symptoms the last 8 weeks, were recruited from elite sport high schools, the website of The Norwegian School of Sport Sciences and through coaches employed at the National Olympic Training Centre (Olympiatoppen) in Oslo, Norway. Only athletes who were able to comply with the study procedures were enrolled. Exclusion criteria were forced expiratory volume in 1 s (FEV_1)<75% or a forced vital capacity <80% according to the Global Lung Function Initiative (GLI 2012),[19] oral corticosteroids or infections in the last 3 months, chronic disease and pregnancy.

Data collection

Electronic questionnaire

Participating athletes received a structured electronic questionnaire by mail on demographic background factors, respiratory health and treatment history, and healthcare utilisation at study enrolment.

Lung function

Dynamic spirometry for the EVH or methacholine BPT was measured by maximal expiratory flow-volume curves (MasterScreen Pneumo Jäger, Würzburg, Germany)[20] according to standardised guidelines from ERS and American Thoracic Society (ATS).[18 21]

For the ECT-related spirometries, the athletes downloaded the CE-marked AsthmaTuner app on their iOS or Android smartphone (MediTuner AB, Stockholm, Sweden). The cloud-based system of AsthmaTuner is described previously,[22] and includes (1) app modules for standardised and unstandardised ECTs connected to a (2) hand-held validated Bluetooth turbine-spirometer (MIR Spirobank Smart, Rome, Italy).[23 24] Spirometry results are presented to the clinician's web interface in real time.[25] The software performs quality controls of lung function manoeuvres in line with the built-in ATS/ERS guidelines, ensuring that the FEV_1 is based on a maximal effort and requires a minimum of three acceptable manoeuvres for an approved test.[21] Reference values for the Jäger and the MIR Spirobank were calculated according to GLI 2012.[19] The athletes were educated on performing a lung function test on the spirometer at inclusion, performing several tests under supervision to ensure proper execution.

Standardised field-based exercise test

Participants performed at least one representative (ie, provoked LAD symptoms) standardised field-based ECT supervised by the app. They were instructed to repeat

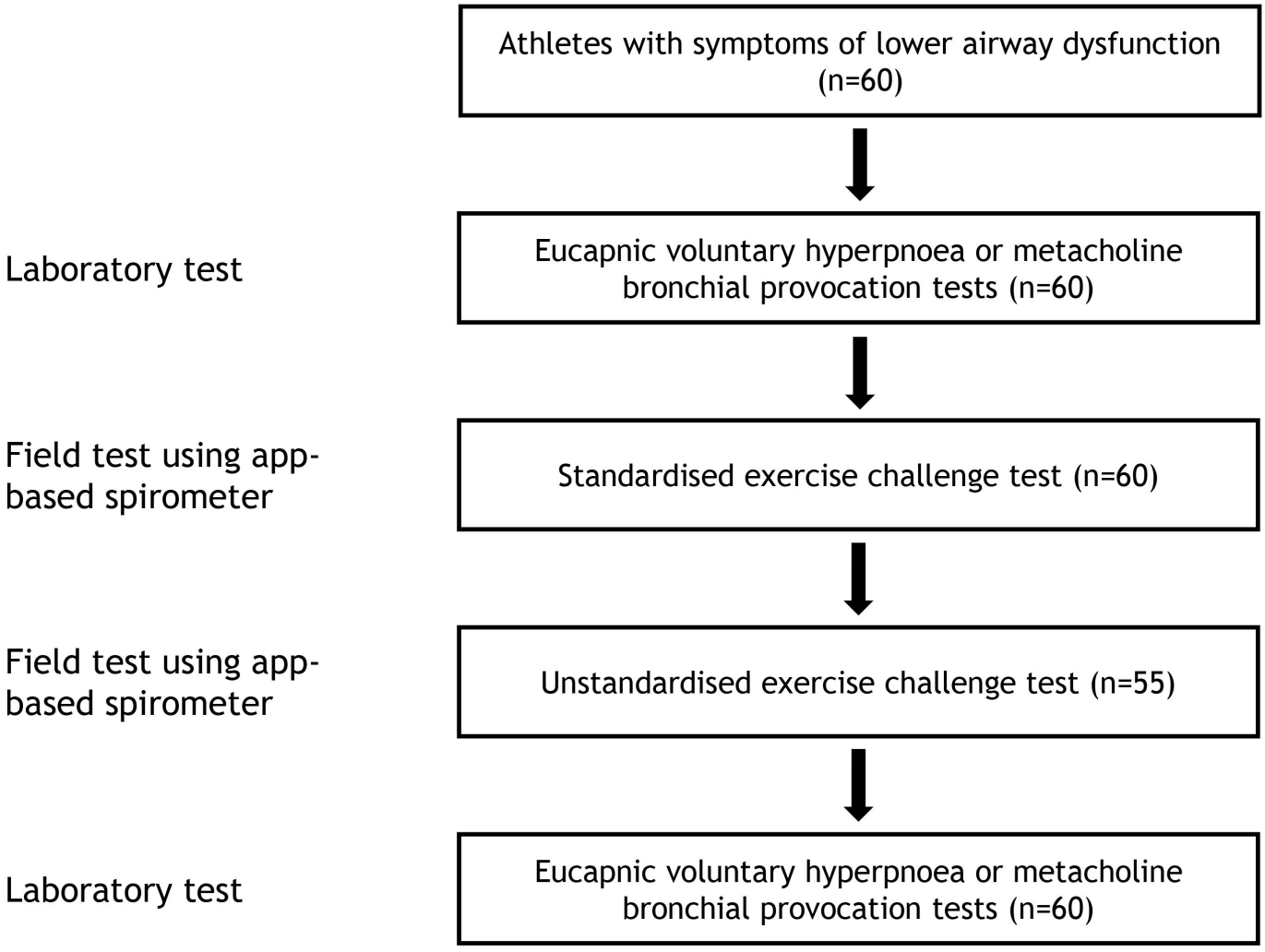

Figure 1 Flow chart showing the bronchial provocation tests included in the study.

the ECT if no LAD symptoms occurred to reduce the risk of false negative results. Ambient conditions and age-predicted maximal heart rate (HR) were registered in the app prechallenge. To secure standardisation, no warm-up was allowed before high-intensity exercise requiring ≥85% of maximal HR for 8 min. HR was measured using an HR-monitor and registered in the app immediately postchallenge. Measurements of FEV_1 were conducted prechallenge and 1 min, 3 min, 5 min, 10 min, 15 min and 30 min postchallenge using the app-based spirometer. The ECT was deemed positive by a ≥10% drop in FEV_1 at two consecutive time points postchallenge.[18] Perceived LAD symptoms were registered at the same time points postchallenge to capture information about symptom presence.

Unstandardised field-based sport-specific exercise test

Participants performed at least one representative unstandardised (ie, any sport or competition) field-based sport-specific ECT and were instructed to repeat the ECT if no LAD symptoms occurred. The app-based spirometer was used prechallenge and at least once within 10 min postchallenge. The ECT was deemed positive by one single ≥10% drop in FEV_1 postchallenge, in line with most previous papers including such unstandardised field-based ECTs.[26–32]

Eucapnic voluntary hyperpnoea

According to standardised protocols, a minute ventilation (V_E) at a target of 85% of maximal voluntary ventilation (FEV_1X30) was secured by continuously measuring expired flow throughout 8 min EVH, the same duration as for standardised ECT.[12 33 34] The athletes breathed a gas mixture of 21% O_2, 5% CO_2 and 71% N_2 from two gas cylinders via a commercial system (EucapSys SMTEC, Switzerland). The FEV_1 was recorded prechallenge and 1 min, 3 min, 5 min, 10 min, 15 min, 20 min, 25 min and 30 min postchallenge, and the EVH was deemed positive by a ≥10% drop in FEV_1 at two consecutive time points postchallenge.[18]

Methacholine BPT

According to ATS guidelines,[32] inspiration-triggered nebuliser (MasterScreen Pneumo Jäger, Würzburg, Germany) delivered methacholine in doubling doses until a ≥20% drop in FEV_1 was observed. Linear interpolation

on the semilogarithmic dose-response curve was used to calculate the accumulated provocation dose (PD_{20}) causing 20% drop in FEV_1, and the methacholine BPT was deemed positive by PD_{20}<4 µmol.[35]

Definitions and outcomes

We defined a confirmed LAD diagnosis as a positive BPT, that is, standardised ECT, unstandardised ECT, EVH or methacholine test, in athletes with a history of LAD symptoms.

Athletes without a confirmed LAD diagnosis were referred to further clinical examinations if indicated based on their symptom presentation.

Data synthesis and analysis

Sample size calculations were based on data provided by Rundell *et al*,[30] reporting that the mean of the pairwise differences between ECT and EVH is 0.014 percentage points, with an SD of 8.35 percentage points. We estimated that with a drop-out rate of 10%, including 60 athletes would provide a power of 80% at a 5% significance level.

Baseline characteristics are reported as means with 95% CIs, except age which is reported in median (range) for continuous data, while categorical data as the number of cases (n) with percentage (%). Potential differences between groups were analysed using Pearson's χ^2 test for categorical data, and the Mann-Whitney U test for continuous data, as these were skewed.

A diagnostic random effects (DerSimonian and Laird) model with a correction factor of 0.5 (only applied to cells where a 0 was present) was used for the sensitivity and specificity analyses, also presented with 95% CI. Since there is no gold standard BPT to confirm LAD, separate analyses were performed for each test comparing with the others as 'reference': (1) standardised ECT, (2) unstandardised ECT, (3) EVH, (4) methacholine BPT. All other statistical analyses were performed with the research platform Ledidi Core.[36]

Patient and public involvement

Athletes and the public were not involved in the design or conduct of this study.

Equity, diversity and inclusion statement

The study team consisted of junior and senior researchers from different disciplines, balanced in gender and age. The study population included male and female athletes from different sports at amateur and professional level. Potential participants may have been excluded due to geographical distances.

RESULTS

Baseline characteristics

Of 60 athletes (median age 17.5, range 16–28 years, 40% females) with LAD symptoms, 67% represented winter sports, 15% swimmers, 43% reported asthma diagnosis and 37% used inhalation corticosteroids and eventual other asthma medications (table 1). All athletes completed the standardised field-based ECT, EVH and methacholine BPT, while five did not complete the unstandardised field-based sport-specific ECT (figure 1). An average of 1.3 (95% CI 1.2 to 1.4) standardised ECTs and 2.9 (95% CI 2.4 to 3.4) unstandardised ECTs were performed to elicit LAD symptoms, and 10 athletes performed more than 2 ECTs.

At least one positive BPT (ie, standardised ECT, unstandardised ECT, EVH or methacholine BPT) was observed in 68% (n=41) of the athletes. Baseline characteristics are reported in table 1 for athletes with or without at least one positive BPT to confirm the LAD diagnosis. Among 19 athletes (32%) without LAD, 2 athletes presented inspiratory breathing symptoms during EVH, were referred to continuous laryngoscopy during exercise and diagnosed with exercise-induced laryngeal obstruction. One athlete had a history of recurrent chronic bronchitis, was referred to bronchoscopy and diagnosed with tracheobronchomalacia (n=1). The 16 athletes without LAD had no clinical presentation indicating further referral.

Ability to detect LAD

Figure 2 demonstrates the ability of the BPTs to objectively detect LAD. In athletes with confirmed LAD, the standardised or unstandardised ECT was positive in 51% (n=21/41) and 49% (n=20/41) of the cases, respectively, while EVH and methacholine BPT each were positive in 32% (n=13/41). In 59% (n=24/41) of the LAD-confirmed athletes, ECTs were the only positive BPT, while both standardised and unstandardised ECTs were positive in 20% (n=7/35) of these athletes. The mean drop in FEV_1 post-challenge for a positive EVH was 16% (95% CI 10% to 22%), for positive standardised ECTs 20% (95% CI 17% to 22%) and positive unstandardised ECTs 15% (95% CI 13% to 17%). Time courses for FEV_1 (l) in positive ECTs are demonstrated in figure 3.

The standardised ECT activity chosen was running 73% (n=44), cross-country skiing 18% (n=7), cycling 7% (n=4) and rowing 2% (n=1). The weather during the standardised ECT was sunny 43% (n=26), cloudy 43% (n=26), foggy 5% (n=3), snowy 5% (n=3) and windy 2% (n=1). The outdoor temperature ranged from −10°C to 10°C in 86% (n=18/21) of the positive standardised ECTs and 74% (n=29/39) of the negative standardised ECTs (p=0.06, χ^2 test). For the unstandardised ECTs, weather, temperature, workload and intensity were not reported since they aimed to assess the actual impact on lung function during sport-specific training sessions in their natural environment.

Diagnostic test performance

Tables 2 and 3 present the sensitivity and specificity of the different BPTs. Standardised and unstandardised ECTs confirmed LAD with 54% (95% CI 25% to 81%) sensitivity and 70% (95% CI 55% to 83%) specificity and 46% (95% CI 19% to 75%) sensitivity and 68% (95% CI 53% to 81%) specificity, respectively, with similar results regardless of reference. In comparison, EVH and methacholine

Table 1 Baseline characteristics of athletes with and without a confirmed diagnosis of lower airway dysfunction (LAD)

Baseline characteristics	LAD diagnosis (n=41)	No LAD diagnosis (n=19)	P value
Age (median, range)	17 (16–27)	18 (16–28)	0.80
Female gender (n, %)	17 (41.5)	7 (36.8)	0.96
Training hours per week (mean, 95% CI)	16.1 (14.9 to 17.4)	15.6 (13.1 to 18.5)	0.37
Type of sport (n, %)			
Winter sports	26 (63.4)	14 (73.7)	0.44
Summer sports*	6 (14.6)	3 (15.8)	0.44
Swimming	8 (19.5)	1 (5.3)	0.44
Football/handball	1 (2.4)	–	–
Other	1 (2.4)	–	–
Ever had rhinitis (n, %)	20 (48.8)	7 (36.8)	0.70
Inhalation allergy (n, %)	22 (53.7)	8 (42.1)	0.58
Ever had eczema (n, %)	15 (36.7)	4 (9.8)	0.44
Current asthma (n, %) Physician-diagnosed asthma (n, %)	21 (51.2) 20 (48.8)	5 (12.2) 4 (9.8)	0.13 0.13
Current use of asthma medication, including ICS (n, %)	20 (48.8)	2 (10.5)	0.67
Respiratory symptoms (n, %)			
Cough (wet or dry)	31 (75.6)	16 (84.2)	0.52
Slime/mucus	38 (92.7)	17 (89.5)	0.67
Heavy breathing/cannot get enough air	32 (78.0)	9 (22.0)	0.13
Wheezing	18 (43.9)	6 (31.6)	0.41
Chest pain	21 (51.2)	8 (42.1)	0.59
Inspiratory stridor/something blocks the throat	32 (78.0)	11 (57.9)	0.13

*Running (LAD vs no LAD; 1 vs 2), rowing (1 vs 1), cycling (2 vs 0), sailing (2 vs 0).
ICS, inhalation of corticoid steroids.

BPT were 33% sensitive (95% CI 15% to 57%) and 85% (95% CI 70% to 94%) specific against standardised ECT as a reference.

DISCUSSION

In this study on 60 athletes with LAD symptoms, a positive BPT confirmed the LAD diagnosis in 41 cases (68%). In 24 of these (59%), the novel concept of using an app-based spirometer for unsupervised standardised and/or unstandardised field-based ECTs was the only positive BPT, but with overlap between standardised and unstandardised ECTs in only 20% of the cases.

The 68% prevalence of confirmed LAD diagnosis in symptomatic athletes is higher than in most previous studies,[9–11 37] including the 22% prevalence reported in a recent systematic review of LAD in athletes.[2] This discrepancy may be explained by the high proportion of winter endurance athletes and pool-based swimmers in our study population, as previous papers including similar populations report up to 70% prevalence of LAD.[2 29 34 38]

Detecting LAD in symptomatic athletes with unsupervised field-based ECTs

The large proportion of confirmed LAD in our study is mainly explained by the 59% of BPT positive athletes who had a positive ECT only. First, one could question if this finding results from the technology failure of the app-based turbine-spirometer. Degryse *et al*[23] validated supervised manoeuvres on a turbine spirometer with similar technology against a daily calibrated Jäger MasterScope as a reference standard. The correlation between 908 parallel measurements on 34 different patients was good (r^2=0.95), and the authors concluded that the Jäger device and the turbine spirometer could be used interchangeably.[23] Second, the reliability of unsupervised lung function manoeuvres is secured through the strict built-in ATS/ERS guidelines.[20] A study including 7777 spirometries,[39] spirometries assessed by computers with built-in guidelines rejected more less valid manoeuvres than human reviewers. The reliability is further supported by (1) the finding of an expected, smooth curve demonstrating at least two consecutive drops in FEV_1 of ≥10% postchallenge in all athletes with a positive standardised ECT (figure 3) and (2) the significant correlation observed between positive standardised ECTs

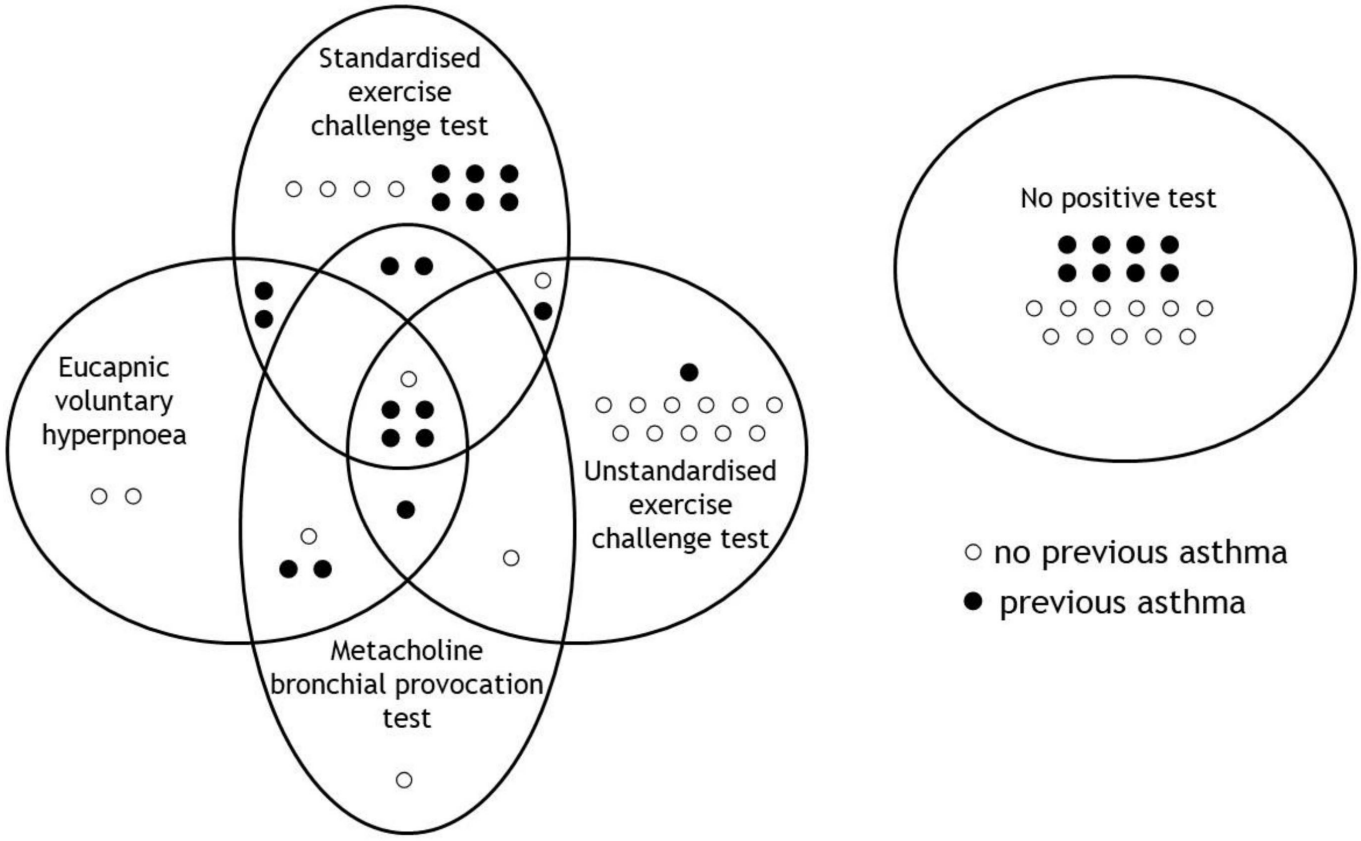

Figure 2 Venn diagram illustrating athletes with a positive eucapnic voluntary hyperpnoea test, methacholine bronchial provocation test), standardised or unstandardised field-based exercise challenge test. Closed circles represent athletes with a current asthma diagnosis, and open circles represent athletes with a previous asthma diagnosis.

and positive EVH. Third, the BPT chosen is important as they differ in test performance. Field-based and sport-specific ECTs are reported as superior to laboratory ECTs,[30] and superior to EVH and methacholine BPTs in detecting exercise-induced airway narrowing,[14] probably because of the impact of ambient conditions. The limited overlap between the standardised and unstandardised ECTs may result from the less strict criteria for a positive unstandardised ECT as compared with the standardised ECTs (one single vs two consecutive ≥10% drops in FEV_1 postchallenge). However, differences in workload and intensity may also play a role, and one may speculate if standardising ECTs can result in a weaker stimulus to elicit LAD. Lack of overlap has been demonstrated between several different BPTs, which emphasises why performing different BPTs is important when LAD is suspected.[14] Finally, the app-based spirometer facilitates regular testing of the fluctuating condition of LAD; exercise-induced airway narrowing is often normalised after a few weeks of rest.[40 41]

Diagnostic test performance

The sensitivity and specificity for documenting LAD with the field-based standardised and unstandardised sport-specific ECTs were 54% and 70%, and 46% and 68%, respectively. Compared with the ECT 51% sensitivity and 84% specificity of ECTs in a recent systematic review on BPT test performance in confirming LAD in athletes,[14] our findings demonstrated a similar sensitivity and a somewhat lower specificity. Cool outdoor temperature ranged from −10°C to 10°C for most of the positive standardised ECTs and may have improved ECT sensitivity, as cool air is reported to improve test performance.[42]

For both EVH and methacholine BPT to document LAD in this study, the sensitivity and specificity were 33% and 85%, respectively, while in a recent systematic review,[14] the sensitivity and specificity for EVH were 46% and 74%, respectively, and for methacholine BPT they were 55% and 56%.[14] The somewhat poorer sensitivity and higher specificity in this study may result from our strict criteria for a positive EVH; two consecutive drops of ≥10% in FEV_1 postchallenge, while several studies require one single drop of ≥10% in FEV_1 postchallenge.[32 34 43 44] For the methacholine BPT the explanation may be the same based on our strict requirement of PD_{20}<4 µmol for a positive test, while diagnostic cut-off levels range from 4 to 9.47 µmol in previous studies.[14 32 45–47]

Limitations

A challenge when comparing different BPTs performances to confirm LAD in athletes is that no gold standard exists as a reference. Even though EVH and methacholine BPTs had the highest specificity, ECTs had

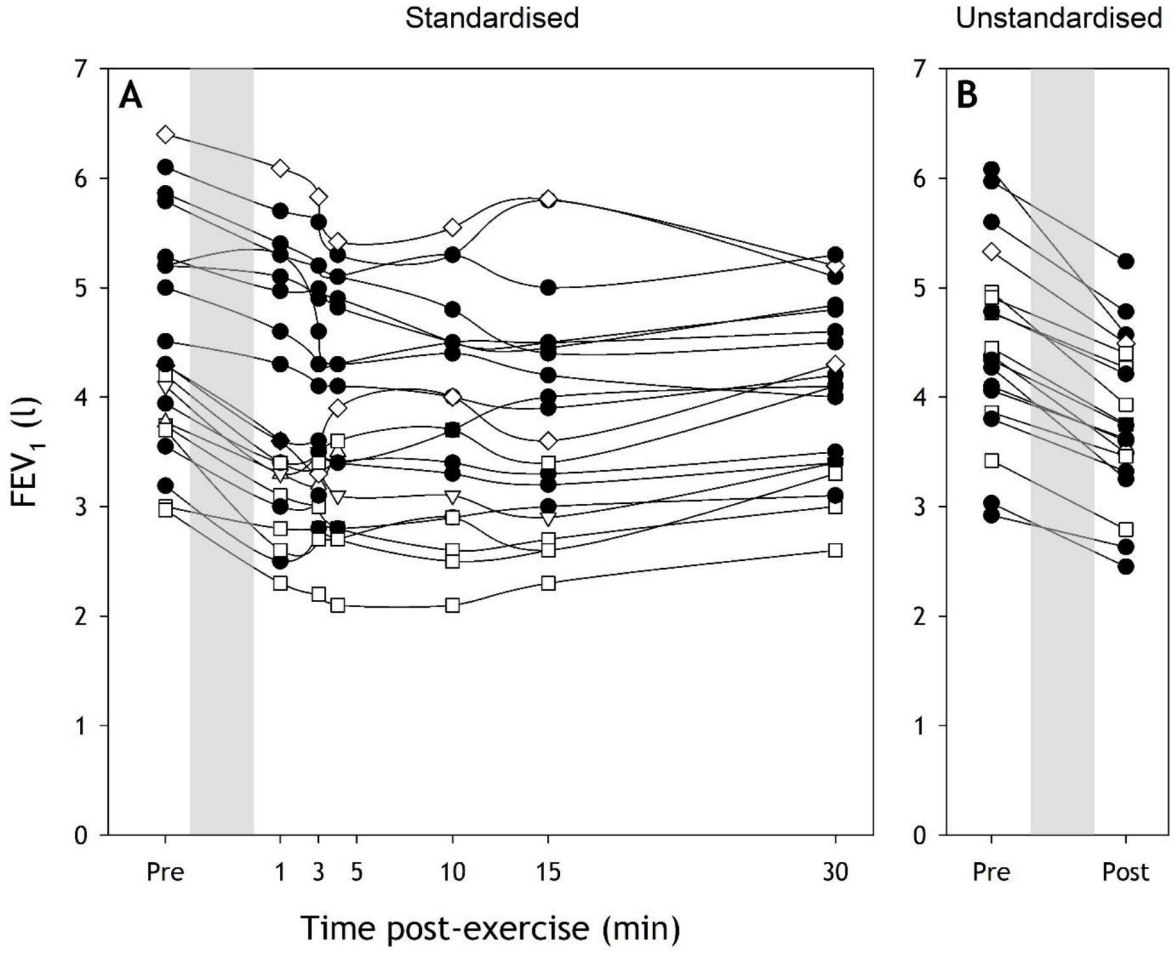

Figure 3 Time course FEV_1 (l) from pre-exercise to postexercise for cases with a positive standardised (left, A, n=21) or unstandardised (right, B, n=20) field-based exercise challenge test. Closed symbols: Athletes with a negative eucapnic voluntary hyperpnoea and methacholine bronchial provocation test. Open symbols: Athletes with a positive eucapnic voluntary hyperpnoea test (diamonds), a positive methacholine bronchial provocation test (triangles) or both tests positive (squares). FEV1, forced expiratory volume in 1 s.

the highest sensitivity, which is preferable to ensure early detection and allow initiation of appropriate treatment.

Using an app-based spirometer is that technology or network may fail. Also, the method relies on the athletes to ensure that HR is sufficient and that exercise is continuous. Education on lung function performance on the app-based spirometer is particularly important for unsupervised tests.

For the unstandardised ECTs, a strategy with two time points rather than one single drop in $FEV_1 \geq 10\%$ postchallenge would have increased test reliability. We suggest that if unstandardised ECTs are used to diagnose LAD, several positive tests with consistent results are needed, to reduce the risk of both false negative and false positive tests.

Table 2 Sensitivity analyses (%) for lower airway dysfunction in athletes using each test as the reference standard (value with 95% CI)

	Reference standard			
Comparator test	**Std ECT**	**Ustd ECT**	**EVH**	**Methacholine BPT**
Std ECT	–	33.3 (14.6 to 57.0)	53.9 (25.1 to 80.8)	53.9 (25.1 to 80.8)
Ustd ECT	33.3 (14.6 to 57.0)	–	46.2 (19.2 to 74.9)	53.9 (25.1 to 80.8)
EVH	33.3 (14.6 to 57.0)	28.6 (11.3 to 15.2)	–	69.2 (38.6 to 90.9)
Methacholine BPT	33.3 (14.6 to 57.0)	33.3 (14.6 to 57.0)	69.2 (38.6 to 90.9)	–

BPT, bronchial provocation test; EVH, eucapnic voluntary hyperpnoea; Std ECT, standardised field-based exercise challenge test; Ustd ECT, unstandardised ECT.

Table 3 Specificity analyses (%) for lower airway dysfunction in athletes using each test as the reference standard (value with 95% CI)

	Reference standard			
Comparator test	**Std ECT**	**Ustd ECT**	**EVH**	**Methacholine BPT**
Std ECT	–	64.1 (47.2 to 78.8)	70.2 (55.1 to 82.7)	70.2 (55.1 to 82.7)
Ustd ECT	64.1 (47.2 to 78.8)	–	68.1 (52.9 to 80.9)	70.2 (55.1 to 82.7)
EVH	84.6 (69.5 to 94.1)	82.1 (66.5 to 92.5)	–	91.5 (79.6 to 97.6)
Methacholine BPT	84.6 (69.5 to 94.1)	82.1 (66.5 to 92.5)	91.5 (79.6 to 97.6)	–

BPT, bronchial provocation test; EVH, eucapnic voluntary hyperpnoea; Std ECT, standardised exercise challenge test; Ustd ECT, unstandardised ECT.

Clinical implications

By including actual ambient conditions, workload and intensity that affect lung function, and by enabling several tests for the fluctuating condition of LAD, this study demonstrates that unsupervised standardised and unstandardised field-based ECTs can support LAD diagnostics in athletes. However, future studies should include supervised ECTs with calibrated spirometers to verify the results. The app-based spirometer is easily available and at low cost, which may reduce the worldwide gap in access to appropriate assessment for LAD-symptomatic athletes.

Conclusion

This study indicates that using an app-based spirometer for unsupervised field-based ECTs in athletes with LAD symptoms can support the diagnostic process for the fluctuating condition LAD.

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Acknowledgements We thank the participating athletes for their cooperation and time. We also thank our nurse, Berit Lian Berntzen, for her contributions.

Contributors Conception and design: TR-N, JSS, MI and BN. Analysis and interpretation: TR-N, MI and RB. Drafting the manuscript for important intellectual content: TR-N, JSS, MI, BN and RB. TR-N confirmed full responsibility for the content of the manuscript.

Competing interests TR-N is employed as a part-time consultant in MediTuner, MI is employed by Medituner, while BN and HL have founded MediTuner, the company owning the medical device AsthmaTuner.

Patient and public involvement Patients and/or the public were involved in the design, or conduct, or reporting, or dissemination plans of this research. Refer to the Methods section for further details.

Patient consent for publication Not applicable.

Ethics approval The study was approved by the Regional Committee for Medical and Health Research Ethics in Oslo, Norway (number 76787), and Lund, Sweden (number 2020-02833), and registered at ClinicalTrials.gov, number NCT04275648.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available on reasonable request. All data relevant to the study are included in the article or uploaded as online supplemental information. Data are available on reasonable request.

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REFERENCES

1 Price OJ, Ansley L, Menzies-Gow A, *et al*. Airway dysfunction in elite athletes--an occupational lung disease *Allergy* 2013;68:1343–52.
2 Price OJ, Sewry N, Schwellnus M, *et al*. Prevalence of lower airway dysfunction in athletes: a systematic review and meta-analysis by a subgroup of the IOC consensus group on 'acute respiratory illness in the athlete *Br J Sports Med* 2022;56:213–22.
3 Hallstrand TS, Moody MW, Wurfel MM, *et al*. Inflammatory basis of exercise-induced Bronchoconstriction. *Am J Respir Crit Care Med* 2005;172:679–86.
4 Anderson SD, Kippelen P. Airway injury as a mechanism for exercise-induced Bronchoconstriction in elite athletes. *J Allergy Clin Immunol* 2008;122:225–35;
5 Rundell KW. Effect of air pollution on athlete health and performance. *Br J Sports Med* 2012;46:407–12.
6 Couto M, Stang J, Horta L, *et al*. Two distinct phenotypes of asthma in elite athletes identified by latent class analysis. *J Asthma* 2015;52:897–904.
7 Schwellnus M, Adami PE, Bougault V, *et al*. International Olympic Committee (IOC) consensus statement on acute respiratory illness in athletes part 2: non-infective acute respiratory illness. *Br J Sports Med* 2022:bjsports-2022-105567.
8 Fitch KD, Sue-Chu M, Anderson SD, *et al*. Asthma and the elite athlete: summary of the International Olympic Committee's consensus conference, Lausanne, Switzerland, January 22-24, 2008. *J Allergy Clin Immunol* 2008;122:254–60.
9 Simpson AJ, Romer LM, Kippelen P. Self-reported symptoms after induced and inhibited Bronchoconstriction in athletes. *Med Sci Sports Exerc* 2015;47:2005–13.
10 Weiler JM, Hallstrand TS, Parsons JP, *et al*. Improving screening and diagnosis of exercise-induced Bronchoconstriction: a call to action. *J Allergy Clin Immunol Pract* 2014;2:275–80.
11 Rundell KW, Im J, Mayers LB, *et al*. Self-reported symptoms and exercise-induced asthma in the elite athlete. *Med Sci Sports Exerc* 2001;33:208–13.
12 Anderson SD, Argyros GJ, Magnussen H, *et al*. Provocation by Eucapnic voluntary Hyperpnoea to identify exercise induced Bronchoconstriction. *Br J Sports Med* 2001;35:344–7.
13 Asthma GIf. Global strategy for asthma management and prevention. n.d. Available: https://ginasthma.org/wp-content/uploads/2021/05/GINA-Main-Report-2021-V2-WMS.pdf2021
14 Reier-Nilsen T, Sewry N, Chenuel B, *et al*. Diagnostic approach to lower airway dysfunction in athletes: a systematic review and meta-analysis by a subgroup of the IOC consensus on "acute respiratory illness in the athlete *Br J Sports Med* 2023;57:481–9.
15 Parsons JP, Hallstrand TS, Mastronarde JG, *et al*. An official American Thoracic society clinical practice guideline: exercise-induced Bronchoconstriction. *Am J Respir Crit Care Med* 2013;187:1016–27.
16 Sandsund M, Faerevik H, Reinertsen RE, *et al*. Effects of breathing cold and warm air on lung function and physical performance in asthmatic and Nonasthmatic athletes during exercise in the cold. *Ann N Y Acad Sci* 1997;813:751–6.
17 Langdeau JB, Turcotte H, Desagné P, *et al*. Influence of Sympatho-vagal balance on airway responsiveness in athletes. *Eur J Appl Physiol* 2000;83:370–5.

18 Hallstrand TS, Leuppi JD, Joos G, *et al*. ERS technical standard on bronchial challenge testing: pathophysiology and methodology of indirect airway challenge testing. *Eur Respir J* 2018;52:1801033.
19 Quanjer PH, Stanojevic S, Cole TJ, *et al*. Multi-ethnic reference values for Spirometry for the 3-95-yr age range: the global lung function 2012 equations. *Eur Respir J* 2012;40:1324–43.
20 Miller MR, Hankinson J, Brusasco V, *et al*. Standardisation of Spirometry. *Eur Respir J* 2005;26:319–38.
21 Brusasco V, Crapo R, Viegi G, *et al*. Coming together: the ATS/ERS consensus on clinical pulmonary function testing. *Eur Respir J* 2005;26:1–2.
22 Bjerg A, Ljungberg H, Dierschke K, *et al*. Shorter time to clinical decision in work-related asthma using a Digital tool. *ERJ Open Res* 2020;6:00259-2020.
23 Degryse J, Buffels J, Van Dijck Y, *et al*. Accuracy of office Spirometry performed by trained primary-care physicians using the MIR Spirobank hand-held Spirometer. *Respiration* 2012;83:543–52.
24 Pollard AJ, Mason NP, Barry PW, *et al*. Effect of altitude on Spirometric parameters and the performance of peak flow meters. *Thorax* 1996;51:175–8.
25 Ljungberg H, Carleborg A, Gerber H, *et al*. Clinical effect on uncontrolled asthma using a novel Digital automated self-management solution: a physician-blinded randomised controlled crossover trial. *Eur Respir J* 2019;54:1900983.
26 Carey DG, Aase KA, Pliego GJ. The acute effect of cold air exercise in determination of exercise-induced Bronchospasm in apparently healthy athletes. *J Strength Cond Res* 2010;24:2172–8.
27 Dickinson JW, Whyte GP, McConnell AK, *et al*. Screening elite winter athletes for exercise induced asthma: a comparison of three challenge methods. *Br J Sports Med* 2006;40:179–82;
28 Durand F, Kippelen P, Ceugniet F, *et al*. Undiagnosed exercise-induced Bronchoconstriction in ski-mountaineers. *Int J Sports Med* 2005;26:233–7.
29 Kennedy MD, Steele AR, Parent EC, *et al*. Cold air exercise screening for exercise induced Bronchoconstriction in cold weather athletes. *Respir Physiol Neurobiol* 2019;269:S1569-9048(19)30105-3.
30 Rundell KW, Anderson SD, Spiering BA, *et al*. Field exercise vs laboratory Eucapnic voluntary Hyperventilation to identify airway Hyperresponsiveness in elite cold weather athletes. *Chest* 2004;125:909–15.
31 Stensrud T, Rossvoll Ø, Mathiassen M, *et al*. Lung function and oxygen saturation after participation in Norseman Xtreme Triathlon. *Scand J Med Sci Sports* 2020;30:1008–16. 10.1111/sms.13651 Available: https://onlinelibrary.wiley.com/toc/16000838/30/6
32 Sue-Chu M, Brannan JD, Anderson SD, *et al*. Airway Hyperresponsiveness to Methacholine, adenosine 5-monophosphate, mannitol, Eucapnic voluntary Hyperpnoea and field exercise challenge in elite cross-country skiers. *Br J Sports Med* 2010;44:827–32.
33 Hull JH, Ansley L, Price OJ, *et al*. Eucapnic voluntary Hyperpnea: gold standard for diagnosing exercise-induced Bronchoconstriction in athletes *Sports Med* 2016;46:1083–93.
34 Martin N, Lindley MR, Hargadon B, *et al*. Airway dysfunction and inflammation in Pool- and non-pool-based elite athletes. *Medicine & Science in Sports & Exercise* 2012;44:1433–9.
35 Coates AL, Wanger J, Cockcroft DW, *et al*. ERS technical standard on bronchial challenge testing: general considerations and performance of Methacholine challenge tests. *Eur Respir J* 2017;49:1601526.
36 Ledidi. Available: https://www.ledidi.com/en
37 Clemm HH, Olin JT, McIntosh C, *et al*. Exercise-induced Laryngeal obstruction (EILO) in athletes: a narrative review by a subgroup of the IOC consensus on 'acute respiratory illness in the athlete. *Br J Sports Med* 2022;56:622–9.
38 Bougault V, Turmel J, St-Laurent J, *et al*. Asthma, airway inflammation and epithelial damage in swimmers and cold-air athletes. *Eur Respir J* 2009;33:740–6.
39 Hankinson JL, Eschenbacher B, Townsend M, *et al*. Use of forced vital capacity and forced Expiratory volume in 1 second quality criteria for determining a valid test. *Eur Respir J* 2015;45:1283–92.
40 Helenius IJ, Tikkanen HO, Haahtela T. Occurrence of exercise induced Bronchospasm in elite runners: dependence on Atopy and exposure to cold air and pollen. *Br J Sports Med* 1998;32:125–9.
41 Bougault V, Loubaki L, Joubert P, *et al*. Airway remodeling and inflammation in competitive swimmers training in indoor chlorinated swimming pools. *J Allergy Clin Immunol* 2012;129:351–8,
42 Bolger C, Tufvesson E, Anderson SD, *et al*. Effect of inspired air conditions on exercise-induced Bronchoconstriction and urinary Cc16 levels in athletes. *J Appl Physiol (1985)* 2011;111:1059–65.
43 Dickinson J, McConnell A, Whyte G. Diagnosis of exercise-induced Bronchoconstriction: Eucapnic voluntary Hyperpnoea challenges identify previously Undiagnosed elite athletes with exercise-induced Bronchoconstriction. *Br J Sports Med* 2011;45:1126–31.
44 Leahy MG, Peters CM, Geary CM, *et al*. Diagnosis of exercise-induced Bronchoconstriction in swimmers: context matters. *Med Sci Sports Exerc* 2020;52:1855–61.
45 Holzer K, Anderson SD, Douglass J. Exercise in elite summer athletes: challenges for diagnosis. *J Allergy Clin Immunol* 2002;110:374–80.
46 Stensrud T, Mykland KV, Gabrielsen K, *et al*. Bronchial Hyperresponsiveness in skiers: field test versus Methacholine provocation *Med Sci Sports Exerc* 2007;39:1681–6.
47 Bohm P, Hecksteden A, Meyer T. Impact of a short-term water abstinence on airway Hyperresponsiveness in elite swimmers. *Clin J Sport Med* 2017;27:344–8.