

Conundrums in the breathless athlete; exercise-induced laryngeal obstruction or asthma?

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Funding information

This study received funds from Haukeland University Hospital and University of Bergen

Purpose: Exercise-induced bronchoconstriction (EIB) and exercise-induced laryngeal obstruction (EILO) are the two disorders commonly considered when athletes complain of exertional dyspnea. They are highly different but often confused. We aimed to address this diagnostic challenge and its consequences in elite athletes.

Methods: We included all athletes competing at national or international level, referred to our institution for workup for EILO during 2013–2016. We diagnosed EILO from video-recorded laryngoscopy performed during maximal cardiopulmonary treadmill exercise (CLE test). Symptoms and previous diagnostic evaluations were obtained from referral letters and chart reviews.

Results: Exercise-induced laryngeal obstruction was diagnosed in 73/101 referred athletes, of whom 70/73 had moderate/severe supraglottic obstruction and 3/73 had primarily glottic obstruction with only minor supraglottic involvement. Of the 73 athletes with EILO, we were able to identify objective tests for asthma in 55 participants, of whom 22 had findings supporting asthma. However, 58/73 had used asthma therapy at some time previously, with current use in 28. Only three reported that asthma medication had improved their exercise-related breathing problems, two of whom with tests confirming asthma. Treatment for EILO improved breathing problems in all but four.

Conclusions: Objective testing verified EILO in most of the referred athletes. EILO coexisting with asthma was common, and large proportions had used asthma medication; however, few reported effect on exercise-related breathing problems. Unexplained persistent exertional dyspnea must not lead to indiscriminate escalation of asthma treatment, but instead incite investigation for EILO, either as a co-morbidity or as a differential diagnosis.

KEYWORDS

continuous laryngoscopy during exercise, EIB, EILO, exercise-induced bronchoconstriction, exercise-induced laryngeal obstruction, vocal cord dysfunction

1 | INTRODUCTION

Respiratory problems are common complaints in athletes. For decades, asthma and exercise-induced bronchoconstriction (EIB) were regarded the most prevailing medical explanation. Proper handling of this scenario was therefore rightly focused in clinical work, research, and sports legislation.^{1,2} We know that EIB diagnosed solely from patient-reported symptoms likely leads to inappropriate conclusions,^{3,4} and guidelines therefore strongly advocate objective diagnostic workup.^{5,6} Regrettably, this is often not done; leading to diagnostic errors and other potentially curable conditions being overlooked.^{7–12}

Exercise-induced laryngeal obstruction or EILO is one of these “other conditions” easily confused with EIB.¹³ EILO is increasingly recognized as a common cause of exertional breathlessness in athletes and physically active individuals, and can objectively be evaluated by laryngoscopy performed continuously during a maximal exercise test, a procedure-labeled continuous laryngoscopy exercise (CLE).^{4,7,14–19} Asthma, EIB, and EILO are not mutually exclusive, but co-exist in an unknown number of patients. Thus, laryngeal abnormalities have been reported to accompany “difficult-to-treat asthma” in a significant proportion, and the relationships between EILO and EIB is debated.^{20,21}

Exercise-related respiratory symptoms in athletes are most often assessed and treated in primary care, and it has been argued that underuse of appropriate evaluation may lead to inaccurate conclusions and missed diagnoses.^{9,22} As asthma is so highly focused in sports medicine, there is a risk that undiagnosed EILO erroneously is perceived as untreated or under-treated asthma, evidently leading to overuse of asthma medication. This again might lead to side effects, doping discussions, and even unwarranted issuing of Therapeutic Use Exemption certificate.²³

We searched our large database of patients referred to our institution for workup for EILO. We aimed to study what fraction of elite athletes referred to our institution, had EILO-diagnosis confirmed when tested with CLE. In athletes diagnosed with EILO, we further addressed how the referring institutions had evaluated respiratory problems prior to the referral, whether asthma medication had been used, and finally how they responded to treatment for EILO.

2 | METHODS

2.1 | Study design and participants

We retrospectively reviewed charts and test results of patients referred to our institution during 2013–2016 for

workup of exercise-induced inspiratory symptoms or exertional dyspnea not responding as expected to asthma treatment, questioning EILO. The inclusion criterion was being an elite athlete (defined as competing at national or international level) with an interpretable video-recorded continuous laryngoscopy during exercise (CLE) test.

Written consent was provided through the “EILO register” at our institution. This register is approved by “The Norwegian data inspectorate” Nr: 12/01063-2/DIJ, and all enrolled patients consent to participate in research. This particular study was approved by the Committee on Medical Research Ethics of Western Norway, no. 2016/1898. User representatives were involved in the design of the protocol and research questions.

2.2 | Continuous laryngoscopy exercise and the definition of EILO

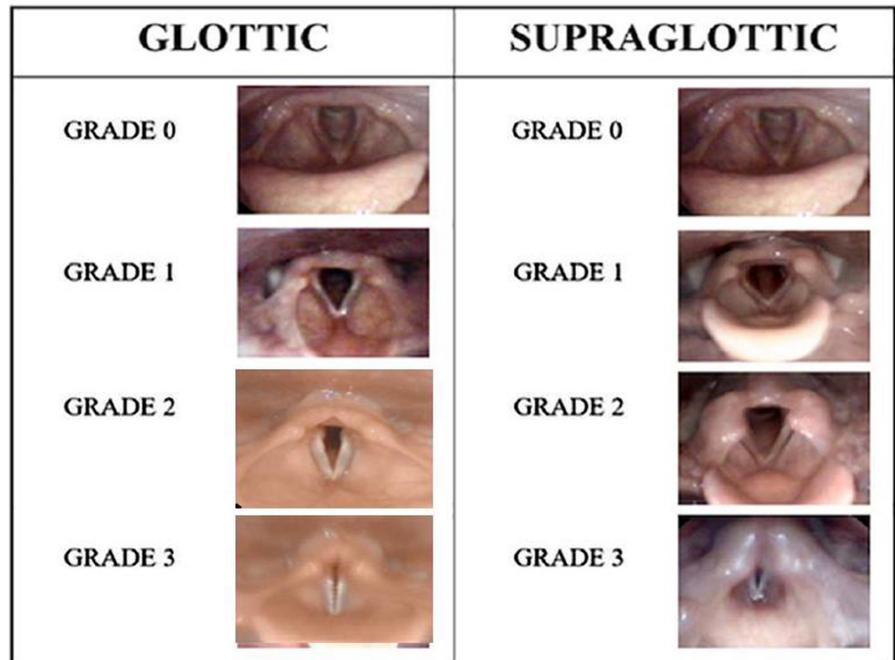
The test has been described in detail elsewhere.¹⁴ Briefly, the patients ran to symptom-limiting distress or exhaustion on a treadmill (Woodway ELG 70), wearing a face mask (Hans Rudolph, Inc.) and a transnasal fiberoptic flexible laryngoscope (Olympus ENF-P3), hooked up to a Jaeger Oxycon Pro Cardiopulmonary Exercise testing system (Viasys Health Care, and a 12 lead ECG [Marquette Medical Systems Inc.]). Data from the CPX unit, the laryngoscope, an external video and sound recorder (Telecam, Karl Storz) were continuously recorded and merged into one file, stored for later evaluation. Treadmill speed and/or grade increased every 1 min, aiming to obtain peak VO_2 after 8–12 min of exercise. The test was considered successful if the patient reproduced his or her respiratory complaints, or indicated exhaustion, preferably supported by a plateau in oxygen consumption and/or the heart rate response.

Laryngeal movements were evaluated using a simplified version of the published CLE scoring scheme.²⁴ Obstruction was scored only at maximal level, and rated as 0–3 at the glottic and the supraglottic level, leaving 6 the theoretical maximal score. A score of 2 or more at the glottic or supraglottic level was required to be diagnosed with EILO (see Figure 1). Three of the authors (JHH, ODR, and HHC) examined all videos independently and in retrospect, blinded to the clinical data, solving disagreements by consensus.

2.3 | Lung function testing

Spirometry was performed at our institution in all participants before the CLE test, using Vmax 22[®] spirometer (SensorMedics).²⁶

FIGURE 1 CLE grading system. Reproduced with permission from Fretheim Kelly et al., *Frontiers in Physiology*²⁵



2.4 | Asthma diagnostics, medication, and respiratory symptoms

The asthma workup was based on information from the referring institutions, reflecting the “real-life-approach” of the study. A positive test for asthma was noted if there were reports of a positive test for salbutamol reversibility exceeding an increase in FEV1 by 12%, and/or a positive test for EIB and/or a positive methacholine provocation test. In some patients, no asthma workup had been done prior to the CLE test. Symptoms were recorded using our standardized in-house questionnaire, where we ask about breathing problem characteristics, such as the duration of the symptoms, when the symptoms occur in the breath-cycle (inspiratory or expiratory) and in relation to exercise sessions (during or after), training intolerance due to symptoms, if breathing difficulties disturb performance, use of asthma medication (past and present), and if asthma medication was perceived as helpful in controlling exercise related symptoms.

2.5 | Treatment for EILO

First line treatment in patients diagnosed with EILO was provided as reassurance and guided breathing advice including breathing exercises performed with the laryngoscope in place, so that patients could observe their own laryngeal responses to the exercises (biofeedback).²⁷ Second line treatment was inspiratory muscle training (IMT)²⁸ or standardized speech therapy. Surgery was offered to carefully selected, highly motivated athletes with

at least moderate supraglottic EILO with an expected significant added benefit from surgery.²⁹ All patients with EILO were offered follow-up evaluations, including a standardized CLE tests.

2.6 | Statistical methods

This was a descriptive study, with main outcomes being CLE-scores, symptom scores, and use of asthma medication, with data reported as means with standard deviations (SD), medians with ranges, or counts with percentages, as appropriate. The CLE-scores are by nature ordinal and categorical, ranging from 0 to 3. Due to the few number of categories, the data were nevertheless reported as means with SDs, as this is considered to provide more information than medians with interquartile ranges. The analyses were performed using SPSS version 24 (SPSS).

3 | RESULTS

The EILO register included 570 patients during the four-year inclusion period, of whom 125 (22%) were classified as elite athletes. We excluded 24 patients for whom we had no consent form, or the film of the larynx was uninterpretable, leaving 101 eligible participants, age range 13–32 (mean 17.8, SD 3.5) years, of whom 18 competing internationally (Table 1). Seventy-five of the 101 reported to exercise every day, 24 exercised 4–6 days a week, and two exercised three days a week.

TABLE 1 Baseline characteristics

Variable (SD)	Females (n = 71)	Males (n = 30)
Age years	17.7 (3.5)	17.9 (3.5)
Height cm	168.8 (6.4)	177.3 (7.3)
Weight kg	60.6 (8.2)	65.8 (11.1)
Distance on treadmill meters	804.7 (152.3)	1138.1 (209.2)
Time on treadmill minutes	11.2 (1.2)	13.5 (1.4)
VO ₂ max ml/min	3084.6 (519.0)	4251.3 (692.1)
VO ₂ max ml/kg/min	50.9 (7.0)	65.0 (7.2)
Minute ventilation L/min	102.6 (17.9)	143.6 (33.1)
MVV L/min	122.7 (24.9)	156.6 (36.4)
Breathing frequencies breaths/min	49.4 (9.2)	53.1 (10.1)
Heartrate beats/min	185 (14.6)	190 (8.9)
FEV ₁ % predicted	111.7 (12.8)	109.5 (11.4)
FVC % predicted	110.9 (12.8)	106.8 (10.6)
Type of sports, n		
Cross country skiing		28
Biathlon		13
Soccer		10
Handball		7
Cycling		8
Swimming		8
Athletics		7
Alpine		4
Bandy		2
Carate		2
Speed skating		2
Others: Orientation, Kayaking, Cheerleading, Figure Skating, Sailing, Nordic Combined, Ballet, Hockey, Rowing, Extreme Sports		10

Note: Figures are means (standard deviations) or numbers.

Abbreviations: FEV₁%, forced expiratory volume at the first second percent predicted; FVC%, forced vital capacity percent predicted; MVV, minute voluntary ventilation (measured); SD, Standard Deviation.

TABLE 2 EILO findings at maximum effort

		Supraglottic obstruction				Total
		0	1	2	3	
Glottic obstruction	0	0	6	6	0	12
	1	1	21	26	0	48
	2	0	3	33	0	36
	3	0	0	3	2	5
Total		1	30	68	2	101

Note: ■ Gray outlines the 73 participants with EILO at maximum effort.

3.1 | Exercise-induced laryngeal obstruction

We diagnosed EILO in 73 of the 101 participants, and in all 18 who competed internationally. Supraglottic

obstruction scored as 2 or 3 was observed in 70/73, and in 15/18 of those who competed internationally (Table 2). In two patients, the supraglottic adduction nearly totally impeded the laryngeal inlet (supraglottic score 3). Glottic (vocal fold) adduction as a secondary phenomenon to the

supraglottic obstruction was observed in 38/73 athletes. Only 3/73 athletes had a predominant glottic adduction, defined by glottic score 2–3 with normal supraglottic score (0 to 1).

3.2 | Symptoms

All athletes reported respiratory symptoms, and 71 of the 73 diagnosed with EILO noted that their respiratory problems prevented them from achieving their goals in their sport, with 29/73 reporting breathing difficulties to be a major problem during competitions. Few (4/73) reported breathing problems during low intensity exercise, compared with 66/73 who reported breathing problems during high intensity exercise. More than half (41/73) noted that their breathing problems could be perceived as a mental strain. Interestingly, only 26/73 informed that their breathing problems had prevented them from “pushing themselves”. The majority (65/73 responders) answered “often to always” when questioned if their respiratory symptoms were worst during inspiration, 49/73 reported stridor, while 17/73 reported problems during expiration (Table 3).

3.3 | Asthma

Of the 73 athletes with EILO, 58 reported to ever have used asthma medication; 15 of the 18 who competed internationally. A positive test for asthma was noted by the referring institution in 22/73, whereas tests for asthma were reported negative for 33/73, and not known or not available in 18/73. CLE test revealed EILO with a supraglottic obstruction grade 2–3 in 56 of the 83 athletes who had used asthma treatment (Table 4). Current (during the past 2–3 months) use of asthma medication during exercise was reported by 27 of the 73 athletes with EILO, eight

of whom competed internationally, of whom one had no positive tests for asthma. Asthma medication was used on a daily basis by 28/73 participants with EILO. Only three of the 73 athletes with EILO reported that asthma medication had been helpful with regard to their exertional breathing problems, two of whom had a positive test for asthma. However, all those three needed additional treatment for EILO (Table 4).

3.4 | Treatment for EILO

Of 73 athletes with EILO, all were given first line treatment, of whom 23 did not need further measures. IMT was provided to 35, and speech therapy to nine athletes. One patient treated with speech therapy needed surgery. Of those treated with IMT, three needed speech therapy and seven additionally needed surgery. Altogether, 14/73 underwent surgery with laser supraglottoplasty. All patients were offered follow-up evaluations, including standardized CLE tests; however, many refused due to no further symptoms or need for follow-up. All but three patients who underwent surgery performed a follow-up CLE test. Nine scored normal, whereas one patient still had EILO but the patient did not want further intervention. Summarized, if we assume that athletes would come for follow-up if they still had problems, treatment for EILO improved exertional breathing problems in all but four athletes.

4 | DISCUSSION

In this selected group of athletes, referred for workup of unexplained breathing problems, we diagnosed EILO in 72%. The majority had a moderate supraglottic obstruction that preceded a subsequent adduction of the glottic folds. A sole glottic obstruction without supraglottic

TABLE 3 Exercise-related respiratory problems by asthma and EILO

	Inspiratory problems	Expiratory problems	Stridor when exercising	Symptoms prevent me from doing exercise	Symptoms prevent me from achieving my goals
Asthma ^b	Never/often/always	Never/often/always	Never/often/always	Never/often/always	Yes/no
Yes	4/11/12	8/13/4	3/10/15	6/10/12	25/1
No	0/16/32	15/19/12	6/21/21	10/18/20	47/0
Unknown	1/5/18	9/10/5	6/6/12	3/12/10	24/1
EILO ^a (73)	6/33/32	32/6/11	23/10/39	13/27/33	71/2

^aEILO; exercise-induced laryngeal obstruction, defined by a glottic or supraglottic score of 2 or more at maximal exercise at continuous laryngoscopy exercise (CLE) test.

^bAsthma diagnosed by referring institute.

TABLE 4 Asthma medication and EILO in relation to presumed asthma

A: All athletes							
	All athletes	Asthma medication			Laryngeal obstruction		
		Ever used	Effect	Current use	No EILO ^a	EILO ^a	Supraglottic obstruction ^b
Asthma ^c :	N = 101	n = 100 yes/no 83/17	n = 66 yes/some/no 4/19/43	n = 98 yes/no 39/59	n = 28	n = 73	n = 70
Yes	28	27/0	3/8/13	20/8	6	22	21
No	48	37/11	1/6/20	10/36	15	33	31
Unknown	25	19/6	0/5/10	9/15	7	18	18

B: Athletes with EILO				
	Athletes w/EILO ^a	Asthma medication		
		Ever used	Effect	Current use
Asthma ^c :	N = 73	n = 73 yes/no 58/14	n = 49 yes/some/no 3/14/32	n = 70 yes/no 28/42
Yes	22	21/0	2/5/13	15/7
No	33	24/9	1/4/13	6/25
Unknown	18	13/5	0/5/6	7/10

^aEILO; exercise-induced laryngeal obstruction, defined by a glottic or supraglottic score of 2 or more at maximal exercise at continuous laryngoscopy exercise (CLE) test.

^bModerate/Severe supraglottic obstruction, (scored as 2 or 3 at maximal exercise).

^cAsthma diagnosed by referring institute.

involvement was rare. Approximately 30% of athletes with documented EILO also had test results compatible with asthma. Use of asthma medication was common, also in athletes with no test results compatible with asthma and few reported effect on the exercise related breathing problems.

4.1 | Strength and limitations

The major strength of this study lies in the high number of participating high-performing athletes, and that EILO was diagnosed as prescribed by guidelines; that is, continuously visualizing the larynx during a maximal intensity exercise test. An obvious weakness was the “real-world data” approach to the asthma workup; that is, data obtained by retrospective chart reviews and based on tests done at the discretion of the referring institutions.³⁰ Proper asthma workup had not been done in all participants, as the referring practitioners had considered the symptoms highly typical for EILO. Thus, the article reflects real-world diagnostic workup and decision-making.

4.2 | The type of EILO in high-performing athletes

Until recently, EILO was referred to as exercise-induced vocal cord dysfunction (VCD) or paradoxical vocal cord (fold) dysfunction or movement disorder (PVCD, PVFMD).³¹ It is important that clinicians and researchers engaged in in this field of respiratory medicine realize that vocal fold obstruction tends to appear toward the end of an exercise session, even in most patients with a predominantly supraglottic EILO. Thus, what usually will be observed with a laryngoscope introduced *after* stopping of exercise, are adducted aryepiglottic folds *and* vocal folds, understandably but erroneously labeled VCD. Recent studies utilizing continuous laryngoscopy during a full exercise session, have convincingly established the complexity of inducible laryngeal obstruction, and that the vocal folds seem to play a secondary role to supraglottic adduction in the majority.^{32,33} In that respect, this study supports that EILO in elite athletes does not differ from EILO as we see it in patients from non-athletic populations; with supraglottic adduction preceding the glottic adduction.³⁴ However, few athletes

had grade 3 obstructions, possibly explained by selection bias; that is, it might be difficult to sustain the ventilation required for elite performance with grade 3 obstruction. Only three patients, had a predominant glottic EILO with only minor supraglottic involvement, that is, findings that could merit being labeled VCD; this in line with “regular patients” with EILO.³³ Because obstruction in the larynx is intricate, misleading labels such as VCD and PVCD/PVFM have now been abandoned.³⁵

4.3 | The prevalence of EILO in athletes

There are relatively few reports on EILO in athletes, and most lack laryngoscopic confirmation. In 2003, Rundell et al. reported stridor in up to 5% of their athletes, half of them also had EIB. The majority had been treated unsuccessfully with asthma medication. None were examined with a laryngoscope.³⁶ Hanks et al. used laryngoscopy to confirm what they described as VCD in a group of athletes who had the laryngoscope introduced *after* stopping of the exercise.³⁷ They reported findings compatible with EILO in 70%, that EILO was more prevalent than EIB, and that the two coexisted in 37%. In 2013, Marcinow et al. performed laryngoscopy *before and after* (but not during) the exercise test in a selected group of athletes suspected to have EILO.³⁸ They found that 87% had laryngeal obstruction evident from laryngoscopy, 39% had previously been diagnosed with EIA, 85% had been using asthma inhalers, and 68% stopped using inhalers after treatment for EILO. Nielsen et al. performed proper CLE tests in their athletes, and found EILO in 35.2% of the participants, 13.6% with coexisting asthma.⁷ Prevalence rates varying between these studies likely reflects differences between the populations examined, the selection process leading to the workup, and the diagnostic evaluations performed in the studies. Our high ratio of confirmed EILO certainly reflects the selected nature of our patients. The cut-off score for labeling laryngeal obstruction as EILO is debated, and it should be mentioned that if we had applied a *sum-score* of at least two, our number had been even higher. Many of the athletes with lower scores did in fact have symptoms compatible with laryngeal obstruction. EILO diagnostics clearly needs more investigation, but this cannot be solved within the frames of this study.

4.4 | The value of skilled healthcare providers

We see the high rate of positive CLE tests in this study as a tribute to the referring healthcare providers, having

embraced the message needed to differentiate EILO from EIB.^{33,39} This suggests that skilled trainers and healthcare providers who acknowledge laryngeal obstruction as a relevant diagnostic possibility are able to discriminate between EIB and EILO, providing they carefully observe their athletes during ongoing exercise as they develop their symptoms. In a skilled environment, the real value of the CLE test lies in its indispensable importance for choosing correct strategy for treatment and follow-up.^{27–29}

4.5 | EILO and EIB

Asthma and EIB are common disorders in athletes, particularly in endurance sports.⁴⁰ EILO is reportedly almost as common; however, there is a significant degree of confusion between the two.^{7,18} Although objective testing is part of the algorithms for workup in all asthma guidelines, we know this is not always done.^{9,11,22} This is highly unfortunate; as we know that diagnosing asthma based on patient-reported symptoms leads to diagnostic errors, this practice should be avoided.⁶ Hitting the target in asthma treatment can be challenging, and overtreatment has been suggested by several authors.¹⁰ For too long, we had a tendency to perceive patient-reported exercise-related respiratory symptoms as under-treated (or untreated) asthma.²² Asthma and EILO can occur independently, but also as each other's co-morbidities. Treatment differs widely between the two, and correct handling of one entity may leave the other untreated. Evidently, if persistence of respiratory symptoms almost by instinct is seen as expressions of uncontrolled asthma, this can lead to massive overtreatment if symptoms are caused by EILO. Important in this context is that EILO does not always lead to symptoms that are easily interpreted, illustrated by the 14 athletes with EILO in our study reporting they never had stridor (Table 3).

Even if our article focuses specifically on EILO and asthma, it is important to remember that respiratory symptoms in athletes can be related to a range of diverse factors. It is therefore particularly important to adopt a systematic approach when exploring respiratory problems. In a study by Hull et al., the researchers found not only asthma and EILO among their athletes, but also a significant number of participants with sino-nasal problems and breathing pattern dysfunction.⁴¹ In a systematic approach to evaluate respiratory problems in athletes, a CLE test will be beneficial on the same level as a Cardio Pulmonary Exercise Test (CPET); that is, after careful history taking and preferably observation of a symptomatic episode, spirometry, testing for bronchial hyper responsiveness and allergy testing if indicated.

5 | PERSPECTIVES

Medical care of respiratory complaints in elite athletes is complicated. A large proportion of athletes with verified exercise-induced laryngeal obstruction (EILO) had used asthma medication, often despite negative tests for asthma, and few reported that medication improved their respiratory complaints during high intensity exercise. CLE testing verified EILO in most athletes referred for workup, suggesting that a high degree of symptom-based diagnostic accuracy is possible for skilled and well-informed healthcare providers. Most athletes with EILO had tried asthma medication for their exercise related breathing problems, most of them unsuccessfully, including those who probably did have asthma. The study underlines that persistent exercise related respiratory symptoms should lead to careful diagnostic considerations and objective testing, and not to indiscriminate use or escalation of asthma treatment. Exertional breathing problems that fail the expected treatment response to asthma medication must incite investigation for EILO also in athletes, in line with suggestions for military personal and children with “difficult-to-treat asthma”.^{19,42}

ACKNOWLEDGEMENTS

The results of the study are presented clearly, honestly, and without fabrication, or inappropriate data manipulation.

CONFLICT OF INTEREST

The authors have no conflicts of interest to disclose.

AUTHOR CONTRIBUTIONS

Ida Hammer and Hege Clemm conceptualized and designed the study and data collecting instruments, collected data, carried out the analyses, drafted the initial manuscript and revised the manuscript. Thomas Halvorsen, Ola Røksund, John-Helge Heimdal, Magnus Hilland and Maria Vollsæter conceptualized the study, designed the data collection instruments, collected data and reviewed and revised the manuscript for important intellectual content. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

DATA AVAILABILITY STATEMENT

In accordance with the approvals granted for this study by The Regional Committee on Medical Research Ethics and The Norwegian Data Inspectorate, the data files are stored securely and in accordance with the Norwegian Law of Privacy Protection. All relevant data are presented in the paper. Because of the selection of participants, only a subset of the datafile will be made available to interested researches on reasonable request to hsyh@helse-bergen.no providing Norwegian privacy legislation and GDPR

are respected, and that permission is granted from The Norwegian Data Inspectorate and the data protection officer at Haukeland University Hospital.

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How to cite this article: Jansrud Hammer I, Halvorsen T, Vollsæter M, et al. Conundrums in the breathless athlete; exercise-induced laryngeal obstruction or asthma? *Scand J Med Sci Sports*. 2022;32:1041–1049. doi:10.1111/sms.14137