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Review

Evaluation and management of exercise-induced dyspnea in otherwise healthy adolescents and young adults: A critical review

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EDUCATIONAL AIMS

This review will enable the reader to:

- Interpret patients' descriptions of symptoms during exercise.
- Understand the limitation of continuous laryngoscopy during exercise.
- Explain when cardiopulmonary monitoring during exercise is needed.
- Choose the type of exercise testing that is best for your patient.

ABSTRACT

Dyspnea on exertion in otherwise healthy adolescents and young adults is often brought to the attention of a pediatric pulmonologist when it interferes with an athletic activity. Assessment of the cause and management has been controversial. Skilled pediatric pulmonologists may suspect the cause from a careful history, but a more definite diagnosis is needed to provide the most appropriate management. Suspecting that laryngeal obstruction is the major cause, continuous laryngoscopy during exercise has been proposed. However, that method tends to over diagnose laryngeal obstruction and does not consider that the larynx is not the major cause of dyspnea on exertion (DOE). The cause of DOE can generally be best identified by a treadmill test using cardiopulmonary monitoring to determine the physiology associated with reproduced symptoms. Management of DOE requires a specific diagnosis and may involve medication, surgery, or education and training.

Introduction

Dyspnea is the perception of difficulty breathing. It involves a complex psycho-physiologic sensation. People describe dyspnea in different ways. They certainly don't use the word dyspnea. Instead, people will say things such as, "I get tired easily," "I have trouble catching my breath," "I can't take a deep breath," "my throat gets tight," "my chest gets tight," "I can't keep up with the other kids," or simply "I get short of breath when I run." Some of the differences appear to be cultural. Complaints of dyspnea may occur spontaneously and during certain activities. It is the episodic dyspnea induced by physical exertion that is addressed in this review.

While anyone can get dyspneic for many reasons, pediatric pulmonologists can be confronted with a consult regarding a teenage athlete or wannabe athlete who wants to know why he or she has difficulty breathing that causes limitations of their desired activity. Identifying the cause of a patient's complaint of dyspnea on exertion (DOE) may be challenging. There are controversies regarding the causes and methods of testing in otherwise healthy adolescents and young adults. Conclusions vary depending on the method by which the cause of DOE for an individual is determined. Asthma, of course, is always an initial consideration for DOE because of the characteristic of asthma to respond to exercise with bronchospasm. Adrenergic bronchodilators, such as albuterol (salbutamol), can usually block exercise-induced bronchospasm when it's from asthma. Identification of asthma as the cause of exercise-induced asthma can therefore readily be identified by the recognition that DOE is prevented by pre-treatment with an inhaled beta$_2$ adrenergic bronchodilator. Consequently, it is the patient with a complaint of DOE who does not respond to a bronchodilator that requires further evaluation.This review will examine the methodologies used to identify the larynx as a cause of DOE, review the exercise physiology associated with DOE, and discuss the treatment of DOE.

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Upper airway as a cause of dyspnea on exertion

One of the earliest reports of DOE that was not from asthma described 7 elite athletes diagnosed with vocal cord dysfunction [1]. However, only 3 of the patients had laryngoscopic visualization of the vocal cords when symptomatic. Flow-volume (FV) relationships showed that evidence for extrathoracic airway obstruction was inconsistent among the 7 patients (Fig. 1). Consequently, the data does not support vocal cord dysfunction as the cause of DOE for all 7 of the athletes. Instead, masqueraders of vocal cord dysfunction must be considered [2]. The illustrations of pre- and post-FV loops in patient 3 and 5 of Fig. 1 shows no marked decrease in the inspiratory portion of the flow-volume loop. That suggests that exercise-induced dyspnea (EID) is not caused by upper airway obstruction in those two patients.

This early study [1], limited as it appears, nonetheless stimulated interest in the epidemiology of vocal cord and other laryngeal abnormalities that could cause respiratory distress. The term, inducible laryngeal obstruction (ILO), entered the lexicon in 2009 [3] using a scoring system for exercise-induced laryngeal obstruction (EILO) obtained during continuous laryngoscopy described in 2006 [4]. During the exercise, scores from zero to three were based on the extent of transient medial rotation of the aryepiglottic folds and adduction of the vocal cords (Fig. 2). Two observers, blinded from any clinical information, independently did the scoring from a video of the larynx during exercise. Scores were indicated as being made twice, at moderate and maximal exercise. This established four sub-scores ranging from 0 to 3 for glottic and supraglottic adduction. A summary score is derived, and values ≥ 3 correlated with subjective severity of respiratory distress.

This method has subsequently been used in several studies of adolescents and athletes with exercise induced dyspnea [5–8]. These studies operate on the premise that the larynx is the main cause of exercise limitation [9]. However, while laryngeal movements were being observed in the videos, no measure of actual obstruction to airflow was included in those studies.

Three reports from the past year (2023) continued to utilize the same methodology with conclusions supporting continuous laryngoscopy during exercise (CLE) as the means to evaluate DOE. Jeppesen states, "*Clinicians are encouraged to consider exercise induced laryngeal obstruction as a possible diagnosis in patients suffering from exercise-induced respiratory symptoms.*" [6] Using the same methodology, Wells reported that "5.7–7.5 % of the general population" have EILO and "*as high as 34 %*" of young athletes presenting with exercise related dyspnea have EILO [7]. Giraud concluded that CLE-test was "*the gold standard for EILO diagnosis and identification of the dysfunctional upper airway site to provide specific management.*" [8] Perhaps CLE to diagnosis EILO is the pyrite (fools gold) of upper airway assessment.

While the scoring system was shown to correlate with the degree of respiratory distress [3], limited air flow through the larynx was not actually demonstrated, and other causes of dyspnea were not considered, At maximal exercise, fluctuations of the glottic structures may occur concomitantly with the actual cause of respiratory limitation and DOE. Is there clinical relevance to observations based on a scoring system that includes transient adductions of the vocal cords or medial rotations of the cuneiform tubercles in the absence of demonstrating actual decreased inspiratory flow from obstruction?

This conflict between the results of the scoring system from CLE and the absence of documented obstruction was apparent from a presentation at the International Exercise & Breathing Conference held by National Jewish Health in Denver on June 6–7, 2023. One of the presentations included a continuous flow-volume tracing of exercise and the corresponding video of the larynx during peak exercise (Fig. 3). The supraglottis and glottis in that video[1] fluctuate with transient adductions sufficient to match the grades shown in Fig. 2. However, the absence of decreased inspiratory flow on the flow-volume tracing of Fig. 3 indicates that there is no obstruction to inspiratory air flow, regardless of any score obtained from the laryngeal movement observed during the exercise. The presence of dyspnea then cannot be attributed to the upper airway.

In contrast, the concordance of decreased inspiratory air flow is readily apparent when vocal cords adduct fully with every inspiration as is readily seen by the corresponding flow-volume loops (Fig. 4) and video at https://www.milesweinberger.com/copy-of-exercise-induced-dyspnea. Respiratory distress during exercise can then be reliably attributed to vocal cord dysfunction [10].

Etiologic determination of dyspnea on exertion

Since there is reason to be skeptical about the value of CLE as a means of identifying the cause of exertional dyspnea, we present a method that examines the physiology when dyspnea occurs. A standardized approach should be used when otherwise healthy adolescents are referred to a pediatric pulmonary clinic with a chief complaint of dyspnea on exertion [11–13]. Since most are likely to have been initially suspected by their referring physician of having exercise-induced asthma and had failed previous or repeated trials of a pre-exercise bronchodilator, an exercise test should be performed. This routinely involves running on a treadmill while progressively increasing ramp and speed until the patient acknowledges that the dyspnea experienced with exertion is reproduced [12]. Throughout the treadmill exercise, there should be continuous monitoring of O2 utilization, CO2 production, heart rate, respiratory rate, flow-volume loops, minute ventilation, ECG, and oximetry (Fig. 5). A capillary gas for pH and pCO2 (in lieu of an arterial catheter) should be obtained promptly when dyspnea is reproduced. If there is any suggestion of stridor or persistent decrease in inspiratory portion of the flow-volume loops, a flexible nasolaryngoscopy should be promptly performed, if not already continuously monitored, after the symptoms of dyspnea are reproduced. The presence of upper airway obstruction is identified by the decreased inspiratory flow after exercising (see Fig. 4). Vocal cord dysfunction[2] then can be differentiated from other causes of decreased inspiratory flow, laryngomalacia and subglottic stenosis.

Using this methodology, the etiologies of exercise-induced dyspnea were evaluated in children and adolescents referred to the pediatric pulmonology clinic of a major university with a chief complaint of dyspnea on exertion. One hundred and seventeen sequential satisfactory tests over an 8-year period were reviewed [12]. Various causes of exercise limitation were identified (Fig. 6). Laryngeal causes were present in only 15 patients, 13 with vocal cord dysfunction and 2 with laryngomalacia. Fifteen with normal spirometry at rest had an abnormal breathing pattern during exercise with an increased respiratory rate compensating for a lower than predicted maximal tidal volume. This was consistent with chest wall stiffness as described in the Wasserman and Whipp's Principles of Exercise Testing and Interpretation [14] Although chest wall abnormalities that can be associated with chest wall stiffness such as pectus deformities and mild scoliosis were indicated in the medical record for some of these patients, there was not a systematic examination for these potential anatomical abnormalities in this retrospective study.

At the time perceived exertional dyspnea was reproduced on the treadmill, normal physiologic limitation was the most common etiology of DOE in 74 of the 117 (63 %) adolescents (Fig. 6). This limitation is from the presence of lactic acidosis that lowers pH. That stimulates further respiratory effort to lower pCO2 and create respiratory alkalosis to normalize pH. But respiratory effort will already be maxed out and cannot decrease pCO2. The result from the persisting acidosis is a progressive increase in respiratory drive that the patient cannot provide.

[1] https://youtu.be/fdQaHY9lYbw.

[2] https://www.milesweinberger.com/copy-of-exercise-induced-dyspnea.

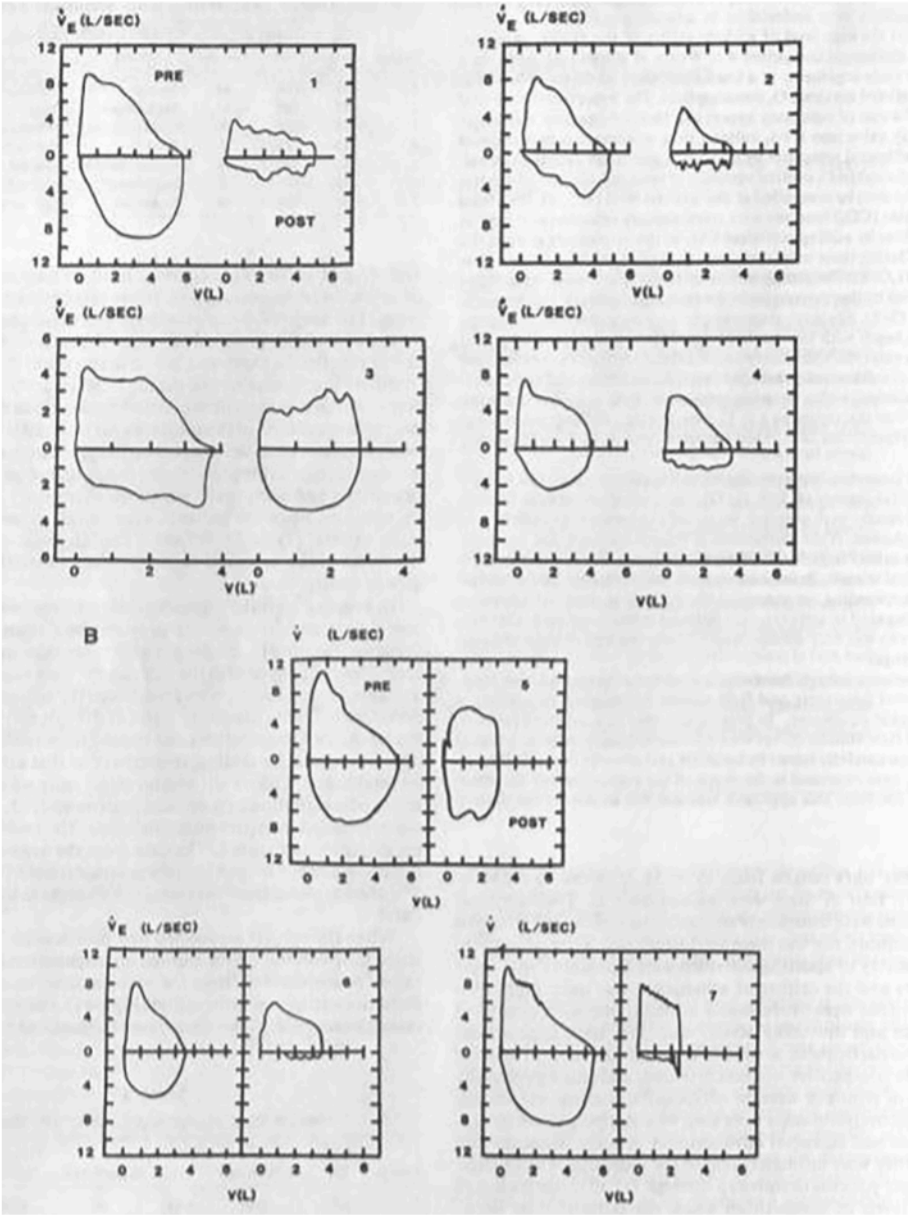

Fig. 1. Flow-Volume (FV) loops of 7 patients pre and post exercise [1]. Patients 2,4,6,7 showed decreased inspiratory flow; this is most commonly from paradoxical vocal cord adduction on inspiration but may also be from laryngomalacia or subglottic stenosis [2]. Patient 1 shows inspiratory and expiratory decrease in flow after exercise that is consistent with persistent adduction of vocal cords. The decreased volumes and other peculiarities on several of the flow-volume loops are not explained.

The inability to meet the demand for increased respiration is perceived as dyspnea by those patients.

Treatment of dyspnea on exertion

Treatment of exercise-induced dyspnea will depend on the specific diagnosis. Exercise-induced laryngeal obstruction (EILO), diagnosed by the method using only continuous nasolaryngoscopy during exercise (CLE), will not reliably identify vocal cord dysfunction as the cause. Exercise-induced laryngeal obstruction is likely to be from vocal cord dysfunction, but it may also be from laryngomalacia [15–17], or even subglottic stenosis [2], both of which would require surgery if clinically needed.

Management of vocal cord dysfunction has included various behavioral methods including therapy by speech and language professionals [18–20]. There was often not a clear distinction in those reports between EIVCD and spontaneous vocal cord dysfunction [21]. Our experience is consistent with other reports that treatment by speech and language professionals provide benefit for spontaneous vocal cord dysfunction [21]. However, the breathing exercises successful for spontaneously occurring vocal cord dysfunction were judged by us to be unrealistic during the typically vigorous peak levels of exercise that precipitate the symptoms of EIVCD. Behavioral methods by speech and language therapists are reported to provide benefit for some with inducible laryngeal obstruction, but multiple sessions are described as being required for benefit, and the duration of effect is not defined [18]. A novel special breathing technique has been described for EILO, but little data is available [22].

During our study of vocal cord dysfunction [21], we considered that the laryngeal nerves that supply the motor and sensory innervation of the larynx was a branch of the vagus nerve [23]. Support for potentially blocking vagal afferents in the laryngeal area was found in two case

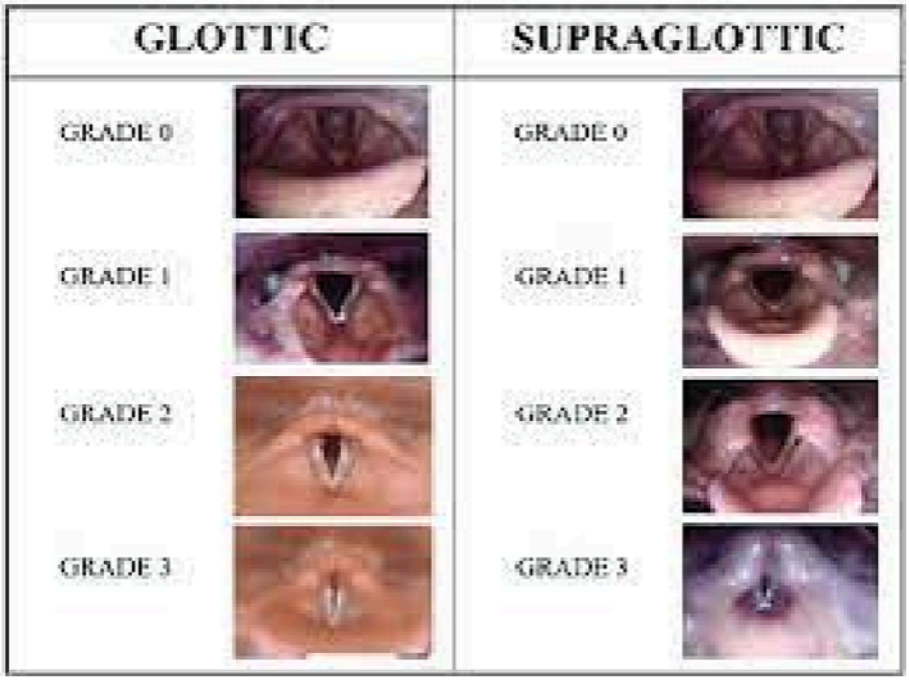

Fig. 2. Scoring system for glottic and supraglottic closure determined by observers of videos obtained with continuous laryngoscopy during exercise. Neither duration of the grades nor concomitant obstruction to airflow was determined [3]. (this version of the original figure in Maat et al [3] from Front Pediatr. 2021;9:617759. https://doi.org/10.3389/fped.2021.617759).

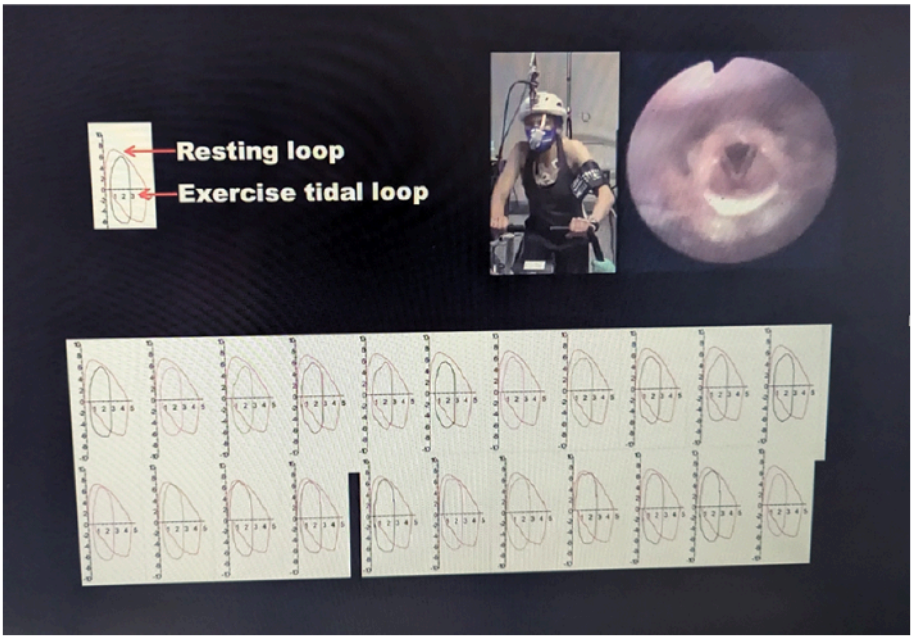

Fig. 3. Flow-Volume loops during exercise with continuous laryngoscopy (obtained from a presentation at the International Exercise & Breathing Conference in Denver June 6–7, 2023). The video of the laryngeal image can be seen at https://youtu.be/fdQaHY9lYbw. That video shows fluctuations of the glottis and supraglottis which is the apparent basis for the scoring described in Fig. 2.

reports that described prolonged use of vagal nerve stimulators, used for intractable seizures, causes vocal cord dysfunction as a complication [24,25]. An editorial also suggested an altered autonomic balance as a cause of vocal cord dysfunction [26]. Speculating that an anticholinergic aerosol might prevent exercise induced vocal cord dysfunction, we tried having the next 6 patients with EIVCD of our VCD study [21] inhale ipratropium from a metered dose inhaler before exercise. Prevention of EIVCD was successful in those 6 patients. Whereas those 6 patients were able to resume activities previously associated with EIVCD, 6 patients in our VCD study prior to our trial of ipratropium continued to have EIVCD and had stopped the activity associated with dyspnea [21]. Although there has been no placebo controlled clinical trial, those limited published observations have been supplemented by subsequent observational experience of the authors. Since there is no experience that imitators of EIVCD [2] will respond to ipratropium, a trial that did not support ipratropium blocking EIVCD [27] based solely on the method of

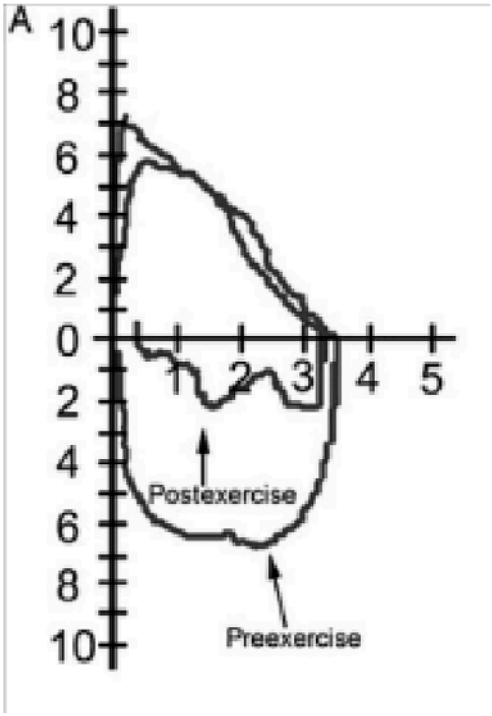

Fig. 4. (A) Flow-volume loop in a 15-year-old.girl with a history of exercise-induced dyspnea. Paradoxical movement of the vocal cords with adduction during inspiration after exercise causes the decreased post-exercise inspiratory flow [10]. The corresponding video can be seen at https://www.milesweinberger.com/copy-of-exercise-induced-dyspnea.

CLE [3] has no credibility.

Breathing dysfunction for those with a decreased maximal vital capacity at maximal exercise increases respiratory rate to maximize minute ventilation. While consistent with chest wall stiffness [14], perhaps in some it is just dysfunctional breathing that might be correctable with training. Patients with dyspnea from vigorous exertion with no abnormality may benefit from counseling involving an age-appropriate explanation of exercise physiology[3] Success at aerobic exercise involves the combination of cardiovascular conditioning and training to learn how to pace at a level that permits completion of the desired activity. An example of that was a 14 y.o. competitive basketball player I encountered. When this physiologic explanation was provided, father said, "But *she can't slow up during the game and be competitive.*" A professional basketball game I watched on TV that evening showed that the players did, in fact, pace themselves by alternating bursts of speed with periods of relatively slow movement. They obviously had learned that behavior to be effective. That was what enthusiastic competitive adolescent athletes with DOE and no physiologic abnormality need to learn.

Discussion

Exercise-induced dyspnea is troubling for adolescents participating in competitive athletics and for those who can't complete usual physical activities. Despite interest and apparent fascination with the components of the larynx, the upper airway is not the major cause of dyspnea on exertion (see Fig. 6). The technique of continuous visualization of the larynx during exercise is interesting but is not a valid means for identifying the cause of exercise-induced dyspnea. The methodology

[3] Older adolescents may have had chemistry in school and had some understanding of pH and acidosis, whereas others required an explanation of those terms and their role in causing exercise limitation.

Fig. 5. 14 y.o. boy on treadmill for exercise test [10].

promoted for evaluation of exercise-induced dyspnea by CLE overinterprets fluctuations of the glottic and supraglottic structures at maximal exercise while not demonstrating actual decrease in inspiratory flow. In contrast, when there is marked decrease in inspiratory flow (Fig. 4), the vocal cords adduct during inspiration instead of the normal abduction necessary for free flow of inspiratory air. Cardiopulmonary monitoring during exercise can identify the respiratory abnormality associated with dyspnea at peak exercise. Identifying the level of cardiovascular conditioning is essential to provide a detailed assessment of the patient's problem.

Conclusion

Pediatric pulmonologists asked to identify the cause of a patient's dyspnea on exertion may hypothesize the cause by a careful history. But

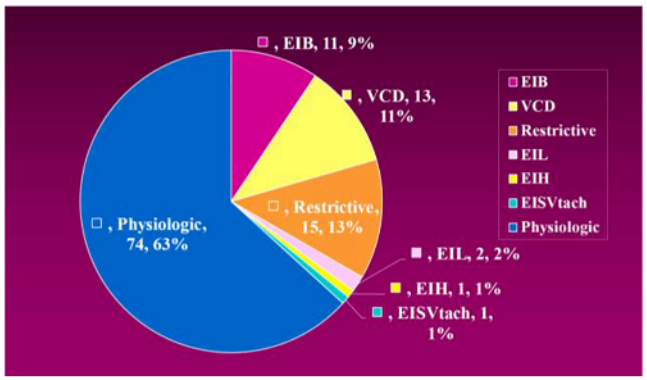

Fig. 6. Causes of exercise-induced dyspnea identified at the time of peak exercise. EIB-exercise-induced bronchospasm, VCD-vocal cord dysfunction, EIL exercise-induced laryngomalacia, EIH-exercise indued hyperventilation, EISVtach- exercise-induced supraventricular tachycardia [10].

that hypothesis can only be tested by determining the pathophysiology at the time of symptom reproduction. Continuous visualization of the larynx during exercise is not a means to identify the causes of dyspnea on exertion. Reproduction of the dyspneic symptoms during cardiopulmonary monitoring can identify the actual cause resulting in a patient's dyspnea on exertion [13].

Future research directions

Studies are needed to verify the pre-exercise inhalation of ipratropium on exercise-induced vocal cord dysfunction suggested by our clinical observations. Our positive experience makes ipratropium the current treatment of choice, but that needs confirmation. An extension of that would include examining the possibility of preventing episodes of spontaneous vocal cord dysfunction by daily maintenance therapy with a long-acting anti-cholinergic aerosol, tiotropium. Studies could examine if patients diagnosed with dyspnea related to what appeared to be restrictive physiology had dysfunctional breathing that could be retrained to have improved minute ventilation by greater maximal tidal volumes instead of increased rate during exercise. Development of lightweight wireless equipment to monitor flow-volume relations, respiratory rate, heart rare, ECG, O2 saturation, oxygen utilization, and carbon dioxide production would provide the ability to assess the physiology associated with dyspnea during the actual activity that precipitates a patient's dyspnea. While aspects of this are technically challenging it could not only be useful for evaluation of exercise-induced dyspnea but could also be useful for athletic training.

Declaration of competing interest

The author declares that he has no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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