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PII: S0091-6749(21)02683-X

DOI: <https://doi.org/10.1016/j.jaci.2021.12.773>

Reference: YMAI 15403

To appear in: *Journal of Allergy and Clinical Immunology*

Received Date: 28 October 2021

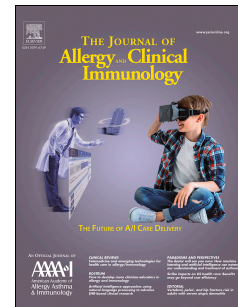
Revised Date: 13 December 2021

Accepted Date: 15 December 2021

Please cite this article as: Hardie WD, Kercksmar CM, Exercise induced laryngeal obstruction: a step in the right direction, *Journal of Allergy and Clinical Immunology* (2022), doi: <https://doi.org/10.1016/j.jaci.2021.12.773>.

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Exercise induced laryngeal obstruction: a step in the right direction

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Disclosure Statement: The authors declare that they have no relevant conflicts of interest.

Key words: exercise, adolescents, stridor, vocal cord dysfunction, patient reported outcome measure

Dyspnea on exertion (DOE) is a common complaint among children and adolescents, and often poses a diagnostic and therapeutic dilemma for the clinician¹. Even after a thorough evaluation including exercise testing, both diagnosis and treatment options may not be clear or straightforward. The potential etiologies can include singular or combined abnormalities in the respiratory, cardiovascular, hematologic, neuromuscular, and psychological systems. Pediatric studies examining the etiologies of dyspnea on exertion consistently identify exercise-induced laryngeal obstruction (EILO) as a leading cause, especially among adolescents and young adult athletes²⁻⁴. Studies suggest a prevalence of EILO confirmed by continuous laryngoscopy during exercise (CLE) among the general adolescent population of 7.5% and 5.7%, respectively and in 26% of those with an asthma diagnosis^{1,5}.

The etiology of EILO is currently unknown, and the disorder is defined by the development of upper airway obstruction during exercise in the absence of associated symptoms at rest. EILO has also been called vocal cord dysfunction (VCD), or paradoxical vocal fold motion, because most obstruction occurs at the level of the vocal cords (Figure); however, the definition is now anatomically broader as obstruction may also occur at the supraglottis from prolapsing arytenoid cartilages, aryepiglottic folds, or epiglottis⁶.

EILO typically presents as exertional dyspnea with a rapid onset and short duration that localizes to the throat with associated inspiratory stridor. However, the clinical presentation of EILO can be highly variable and can occur in combination with other respiratory causes of DOE, including exercise-induced bronchospasm, exercise-induced hyperventilation, and asthma. Baseline pulmonary function testing and exercise challenges are important components essential for assessing DOE but are not specific for diagnosing EILO. Definitive diagnosis of EILO is made through CLE but is typically restricted to specialty centers and interpretation dependent on the expertise of the proceduralist. A variety of medical, behavioral, and surgical treatment options for EILO are purported to be helpful but to date randomized clinical trials do not exist to quantitatively assess the efficacy of these interventions. Currently respiratory retraining directed by a speech pathologist is the mainstay of therapy but is not standardized across centers and evaluation of treatment is primarily subjective. Taken together, EILO is a relatively understudied disorder in need for objective, reproducible, and feasible clinical tools which can evaluate the efficacy of novel therapeutic interventions.

In this issue of *The Journal of Allergy and Clinical Immunology*, Olin and colleagues address this gap by providing a validated, patient-reported outcome measure (PROM) specific to EILO⁷. The authors developed and validated an Exercise-induced Laryngeal Obstruction Dyspnea Index (EILODI) in adolescents and young adults as an instrument for use in clinical trials. The EILODI was developed using comprehensive, well-designed methodology. Experts from several disciplines used an evidence-based approach to identify relevant symptoms and to draft questions. A focus group of 10 patients previously diagnosed with EILO using CLE provided feedback that was used to refine the questionnaire to 20 items. Next, a group of 219 patients previously diagnosed by CLE as having EILO (including 49 with asthma) and a control group of 30 subjects without exertional dyspnea participated in metric evaluation and validation. All items are answered using a 5-point Likert scale with score ranging from 0 to a maximum of 48. Lastly, the EILODI was validated by comparing the EILODI with categorical assessments of disease burden, a binary (yes/no) perception of symptom improvement, and a daily symptom log. The final EILODI is a 12-item questionnaire on frequency, duration, and type of symptoms as well as effects of symptoms on ability to exercise and overall well-being. The average scores of EILO and healthy controls differed significantly (28.8 (SD 7.4) and 4.5 (SD 7.4), respectively). A minimal clinically important difference (MCID) of 6 was determined and there was not a significant difference between EILODI score in the group with concomitant asthma compared to those without.

The EILODI adds to a short list of existing tools to monitor symptoms and response to therapies in individuals with EILO. The 12-item Vocal Cord Dysfunction Questionnaire (VCDQ) was developed in a fashion similar to the EILODI⁸. However, the VCDQ has several potential limitations for use in pediatric patients with dyspnea on exertion. The patient cohort was substantially older (mean age ~50 years), included several patients with chronic lung disease apart from asthma, and did not limit to patients with only exercise as symptom trigger. Although healthy controls and those with asthma alone scored significantly below those with VCD, the VCDQ was not considered a screening or diagnostic tool. The Dyspnea Index (DI) was developed to evaluate the psychophysiological impact and severity of upper airway related dyspnea⁹. This 10-item questionnaire rates responses to questions about noisy breathing, tightness, worsening with exercise and stress caused by breathing difficulties. The DI demonstrated excellent test-re-test reliability across a group with both anatomic and functional obstruction, but like the VCDQ, was developed in a largely adult population.

The EILODI is unique in offering clinical investigators an instrument specifically targeted to measuring temporal changes in symptoms in adolescents and young adults who have documented EILO. As a validated PROM, the EILODI has the potential to encourage and facilitate research into the etiologies, natural history of and treatments for EILO. Clinical trials will draw increased awareness of this common but often under- or misdiagnosed condition. Researchers and ultimately clinicians will have a much-needed instrument to measure change in symptoms in response to existing and newly developed treatments. Of note, the EILODI is intended to monitor change in EILO symptoms but is not a diagnostic tool nor can it distinguish EILO from exercise-induced asthma. In addition, the EILODI will require further testing in research and clinical populations, including wider application to different ethnic groups that are under-represented in the current study. It is certainly possible that cultural or sociodemographic factors could influence the answers to the EILODI questions and affect validity and responsiveness. However, the findings of the Olin team's study provide an important and encouraging step forward in facilitating comparative effectiveness clinical trials and evaluating management options for patients with this common and confounding disorder.

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Figure Legend

Continuous laryngeal endoscopy (CLE) on a 15 year old male with dyspnea on exertion. Left panel demonstrates open glottis early in exercise with glottis closed during intense exercise as patient developed stridor (right panel).

