Continuous laryngoscopy during exercise - proposal for a clinical protocol based on bibliographic review

Review Article

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Abstract

Objectives - Establishment of a protocol for Continuous Laryngoscopy during Exercise (LCE).
Study Design – Systematic Bibliographic Review.
Material and Methods - Bibliographic review in the MEDLINE, Cochrane Central Register of Controlled Trials and Cumulative Index to Nursing and Allied Health Literature databases, based on the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) model, between 2001 and 2021. The studies included in the literature review analyzed LCE protocols in both pediatric and adult ages and were written in English or Portuguese. Articles that only discussed Exercise-Induced Laryngeal Obstruction, but not the LCE protocol and articles whose study objective was not to investigate the results of the LCE protocol were excluded. Based on the results obtained, a clinical protocol was developed for the Centro Hospitalar Universitário Lisboa Central and tested on a group of 10 healthy volunteers.
Results – The search produced a total of 679 articles, and after applying the inclusion and exclusion criteria, 21 studies were selected. In these, there were a total of 1026 patients analyzed, with a male:female ratio of 1:1.7. The average age at which LCE was performed ranged from 9 to 45 years. The preferred exercise method in the protocols studied was the treadmill (n = 17; 81%), followed by the exercise bike (n = 4, 19%) and the rowing machine (n = 1; 4.8%).
The proposed LCE protocol includes a modified Bruce protocol, with LCE ending when patients are exhausted or have limiting respiratory symptoms. Immediately before and after LCE, spirometry was performed. Glottic and supraglottic movements were assessed at rest, with moderate effort and maximum effort, in each phase of the respiratory cycle.
Conclusions - Based on data from a bibliographical review, a protocol for carrying out LCE was developed, demonstrating feasibility and suitability for the reality of a Portuguese institution when tested on healthy volunteers. Further studies with patients are needed to validate these results.
Keywords: Continuous laryngoscopy during exercise, Exercise-induced laryngeal obstruction, Laryngoscopy

Introduction

Exercise-Induced laryngeal obstruction (EILO) is a clinical entity characterized by inappropriate closure of the larynx during physical activity, resulting in the development of respiratory symptoms such as wheezing, dyspnea, and stridor[1].

This condition is a relatively common cause of exertional dyspnea in adolescents and young adults, with a Danish study indicating a positive EILO diagnosis in 7.5% of the population aged between 14 and 24 years[2]. The larynx exhibits an opening movement at both the supraglottic and glottic levels during exercise in asymptomatic individuals[3]. The pathophysiological mechanisms underlying the narrowing of the laryngeal lumen in patients with EILO remain poorly understood. In the context of EILO, the restriction to airflow is solely induced by exercise, meaning that pre- and post-exercise evaluations are seldom informative[3].

The misdiagnosis of asthma in patients with EILO is common due to the overlapping symptoms. The most notable difference is the timing of symptom onset: in EILO, symptoms appear at the peak of physical exertion and subside within minutes, whereas in asthma, symptoms typically emerge post-exercise and dissipate more gradually[4]. Additionally, inspiratory stridor is atypical in asthmatic patients and more commonly observed in those with EILO. It is important to note that the diagnosis of EILO does not encompass conditions involving obstruction of the airways distal to the larynx, such as asthma[5].

Patients with EILO are often underdiagnosed or misdiagnosed, and improperly treated without clinical benefit with beta-2 adrenergic agonists and corticosteroids, thereby exposing them to complications associated with these inhaled treatments[6].

Bronchial provocation tests do not have diagnostic utility for EILO, as direct visualization of the larynx during intense exercise is required[7]. The gold standard for the diagnosis of EILO is continuous laryngoscopy during exercise (CLE), first described by Heimdal et al. in 2006[3]. CLE enables the assessment of the larynx during physical activity, providing crucial insights into the location of laryngeal closure (at the glottic and/or supraglottic level), and can guide subsequent therapeutic management. Despite this diagnostic technique being described over 15 years ago, it remains underutilized in the clinical practice of otolaryngology, and there is significant variability in the protocols adopted internationally.

The current article has been divided into two distinct sections. In the first section, we present the findings of a systematic literature review on various CLE protocols. The second section discusses the development of a protocol for a Portuguese tertiary hospital center, the Central Lisbon University Hospital Center (CHULC), that reflects the best international clinical practices, yet mirrors the reality and resources of Portugal. This protocol was developed based on the findings of the literature review.

Materials and Methods

The literature review was conducted in accordance with the *Preferred Reporting Items for Systematic Reviews and Meta-Analyses* (PRISMA) guidelines[8]. The online databases *MEDLINE*, *Cochrane Central Register of Controlled Trials* (CCRCT), and *Cumulative Index to Nursing and Allied Health Literature* (CINAHL) were searched for the relevant literature. The search was conducted between November 15, 2022 and November 30, 2022, and included studies published between January 2001 to December 2021.

The studies included in the literature review examined CLE protocols in both the pediatric and adult populations, and were written in either English or Portuguese. Articles that solely discussed EILO but did not address the CLE protocol, as well as those that did not investigate the outcomes of the CLE protocol, were excluded. In the first step, duplicate articles were excluded. Subsequently, two independent reviewers assessed the titles and abstracts, excluding publications that did not meet the inclusion criteria. The full text of the remaining articles was retrieved and assessed for eligibility by both the reviewers, who also independently extracted the necessary data. The collected demographic data included sex, age of patients/participants, and body mass index (BMI). The exercise modalities employed in each protocol were also documented: treadmill, stationary bike, or rowing machine. The parameters analyzed across various protocols were recorded, including forced vital capacity (FVC), forced expiratory volume in the first second (FEV1), maximum oxygen consumption (VO2 max), respiratory quotient (RQ), maximum voluntary ventilation (MVV), total lung capacity (TLC), maximum heart rate (HR max), oxygen saturation (SatO2), endoscopic assessment of the supraglottis and glottis, time to onset of EILO, time to exhaustion, and time to symptomatic resolution. The clinical and demographic characteristics, as well as the exercise methods and parameters analyzed in the CLE protocols, are presented through descriptive statistics.

Results

SECTION 1

SYSTEMATIC LITERATURE REVIEW

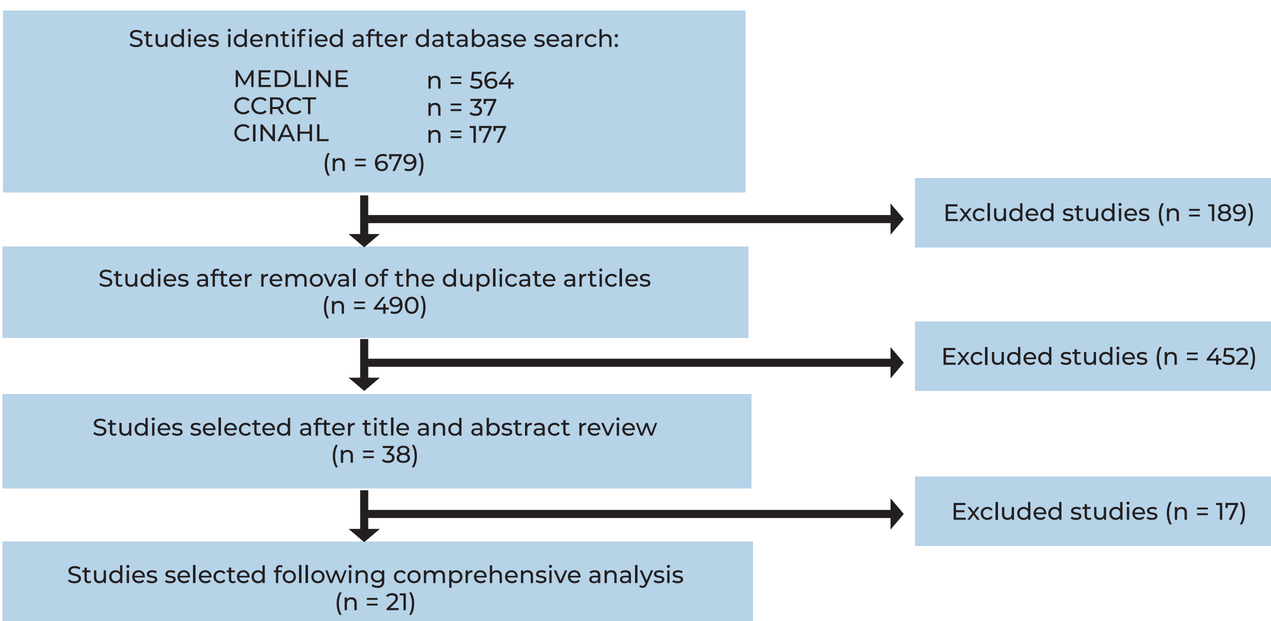
Study Selection

The search in the previously mentioned databases yielded a total of 679 articles (Figure 1). After the removal of duplicate articles, 490 articles were obtained. From these, after reviewing the title and abstract and applying the inclusion and exclusion criteria, 38 articles were selected for full text reading. Finally, following a comprehensive review, 21 studies were selected: 14 prospective cohort studies (66.7%), three retrospective cohort studies (14.3%), two systematic reviews (9.5%), one case series (4.8%), and one case-control study (4.8%) (Table 1). Over half of the articles (81%) were published in or after the year 2011.

Demographic Characteristics

In the 21 studies included, a total of 1026 patients were analyzed, with a male-to-female ratio of 1:1.7. The number of patients in each of the studies ranged from 1 to 150 (Table 1). The average age at which CLE was performed ranged from 9 to 45 years, with a mean age of 20 years and 8 months.

Figure 1
Flowchart for the selection of studies in the literature review in accordance with the PRISMA guidelines. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; CCRCT, Cochrane Central Register of Controlled Trials; CINAHL, Cumulative Index to Nursing and Allied Health Literature.



Assessment of the Studied CLE Protocols

The preferred exercise modality in the studied protocols was the treadmill (n = 17; 81%), followed by the stationary bike (n = 4, 19%) and the rowing machine (n = 1; 4.8%) (Table 1).

In 18 out of the 21 (85.7%) selected articles, the authors refer to the patients' sex in the questionnaire of their protocol, and in 13 (61.9%) to the BMI (Table 2). Spirometry with FVC calculation was performed in 47.6% of the protocols (n = 8), and FEV1 in 57.1% (n = 12). VO2 max was documented in 47.6% of the included articles (n = 8), RQ in 23.8% (n = 5), MVV in 19% (n = 4), TLC in 19% (n = 4), HR max in 71.4% (n = 15), and $SatO_2$ in 23.8% (n = 5) articles. Endoscopic assessment of the supraglottis and glottis was conducted in all studies. The assessment of the time to development of EILO and time to exhaustion was included in the evaluation of four protocols (19%), and the time to symptomatic resolution in just one (4.8%).

SECTION 2
CLE ANALYSIS PROTOCOL AT CHULC

Patient and Equipment Preparation

The ambient temperature of the laboratory is set to maintain a range between 20 and 25°C, with humidity levels kept below 50%. The equipment is calibrated prior to each test in accordance with the instructions provided in the manufacturer's manual.

Table 1
Studies included in the literature review and data of the selected patient population who underwent continuous laryngoscopy during exercise (CLE)

Study (Authors)	Year of Publication	Study Design	Number of Patients (M/F)	Age, years (average and range)	Exercise method
Heimdal et al.[3]	2006	Prospective cohort	16 (10/6)	28.8 (15-29)	Treadmill
Maat et al.[9]	2009	Prospective cohort	100 (27/73)	17.2 (9-44)	Treadmill
Tervonen et al.[10]	2009	Prospective cohort	30 (6/24)	27.8 (10.6–69.2)	Bicycle
Christensen et al.[11]	2010	Prospective cohort	97 (39/58)	18.5 (14-24)	Treadmill
Maat et al.[12]	2011	Retrospective cohort	114 (NR)	NR	Treadmill
Christensen et al.[13]	2013	Prospective cohort	39 (NR)	21.7 (15-34)	Treadmill
Olin et al.[14]	2014	Retrospective cohort	150 (NR)	16.8 (NR)	Bicycle
Panchasara et al.[15]	2015	Case Series	2 (0/2)	21 (20-22)	Rowing
Røksund et al.[16]	2015	Systematic Review	NR	NR	Treadmill
Buchvald et al.[17]	2016	Retrospective cohort	51 (30/21)	13.9 (7-18)	Treadmill
Norlander et al.[18]	2016	Prospective cohort	NR	NR	Treadmill
Olin et al.[19]	2016	Prospective cohort	71 (24/47)	15 (12-21)	Treadmill
Walsted et al.[7]	2016	Prospective cohort	37 (17/20)	26 (15-45)	Treadmill
Mirza et al.[20]	2017	Prospective cohort	11 (1/10)	29 (18-43)	Treadmill or bicycle
Walsted et al.[1]	2017	Case-Control	23 (4/19)	23 (15-45)	Treadmill
Sandnes et al.[21]	2019	Prospective cohort	28 (4/24)	16.4 (12-25)	Treadmill
Ersson et al.[22]	2020	Prospective cohort	75 (NR)	(15-17)	Treadmill
Norlander et al.[23]	2020	Prospective cohort	125 (53/72)	14.9 (13-15)	Treadmill
Engan et al.[24]	2021	Prospective cohort	40 (19/21)	24.8 (15-35)	Treadmill
Giraud et al.[4]	2021	Systematic Review	NR	NR	Treadmill
Word et al.[25]	2021	Prospective cohort	17 (4/13)	16 (9–27)	Bicycle

M, male; F, female; NR, not reported

Table 2
Parameters analyzed in continuous laryngoscopy during exercise (CLE) in the studies included in the literature review

Study (Authors)	Sex	BMI	FVC	FEV1.	VO2 max	RQ	MVV	TLC	HR max	SatO2	Evaluation of Supraglottis	Evaluation of Glottis	Time to EILO	Time to Exhaustion	Time to Resolution
Heimdal et al.[3]	X	X	X	X	X	X	X	X	X	X	X	X	NR	NR	NR
Maat et al.[9]	X	NR	NR	NR	NR	NR	NR	NR	X	X	X	X	X	X	NR
Tervonen et al.[10]	X	NR	NR	X	NR	X	NR	NR	X	X	X	X	NR	NR	NR
Christensen et al.[11]	X	X	NR	NR	NR	NR	NR	NR	X	NR	X	X	NR	NR	NR
Maat et al.[12]	X	NR	NR	NR	NR	NR	NR	NR	X	NR	X	X	NR	NR	NR
Christensen et al.[13]	X	X	NR	X	NR	NR	NR	NR	X	NR	X	X	NR	NR	NR
Olin et al.[14]	X	X	NR	X	X	X	X	X	NR	NR	X	X	NR	NR	NR
Panchasara et al.[15]	X	NR	NR	NR	NR	NR	NR	NR	NR	NR	X	X	NR	NR	NR
Røksund et al.[16]	NR	NR	X	X	NR	NR	NR	NR	NR	NR	X	X	NR	NR	NR
Buchvald et al.[17]	X	X	X	X	NR	NR	NR	NR	X	NR	X	X	NR	NR	NR
Norlander et al.[18]	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	X	X	NR	NR	NR
Olin et al.[19]	X	X	NR	X	X	NR	NR	NR	X	NR	X	X	X	NR	X
Walsted et al.[7]	X	X	X	X	NR	NR	NR	NR	NR	NR	X	X	NR	NR	NR
Mirza et al.[20]	X	X	X	X	X	NR	NR	NR	X	NR	X	X	NR	NR	NR
Walsted et al.[1]	X	X	X	X	NR	NR	NR	NR	X	NR	X	X	X	X	NR
Sandnes et al.[21]	X	X	X	X	X	X	X	X	X	NR	X	X	NR	X	NR
Ersson et al.[22]	X	X	NR	NR	NR	NR	NR	NR	X	NR	X	X	NR	NR	NR
Norlander et al.[23]	X	X	NR	NR	NR	NR	NR	NR	NR	NR	X	X	NR	NR	NR
Engan et al.[24]	X	X	X	X	X	X	X	X	X	X	X	X	NR	NR	NR
Giraud et al.[4]	X	NR	NR	NR	X	NR	NR	NR	X	X	X	X	X	X	NR
Word et al.[25]	NR	NR	NR	NR	X	NR	NR	NR	X	NR	X	X	NR	NR	NR

BMI, body mass index; FVC, forced vital capacity; FEV1, forced expiratory volume in the first second; VO2 max, maximum oxygen uptake; RQ, respiratory quotient; MVV, maximum voluntary ventilation; TLC, total lung capacity; HR max, maximum heart rate; SatO2, oxygen saturation; EILO, exercise-induced laryngeal obstruction; X, performed; NR, not reported.

CLE Setup

A work unit has been established for the performance of CLE, comprising a flexible nasofibrolaryngoscope (with a diameter of 3.6 mm), equipment for cardiopulmonary exercise testing with a treadmill, and video and audio recording materials. A headrest has been designed to secure the fibroscope, camera, and flow sensor during exercise. The patient's upper body is recorded to document the associated movements and any potential respiratory distress, and the respiratory sounds are captured using a microphone positioned near the headrest. This experimental setup was previously tested on a group of 10 adult volunteers and adjusted for optimal technical performance.

A modified *Bruce* protocol with incremental intensity increase every 90 seconds was established. The parameters of pulmonary function were determined by spirometry immediately before and after the completion of CLE, specifically the FVC, FEV1, VO2 max, RR, MVV, and TLC.

Performing the CLE

The nasal cavities are anesthetized with 2% lidocaine gel, 10 minutes prior to the procedure. The nasofibrolaryngoscope is positioned to enable visualization of the epiglottis, supraglottic region, and glottis, and the nasal forceps are applied, remaining in place throughout the entire CLE procedure. Throughout the CLE, the patient is monitored using a 12-lead electrocardiogram and pulse oximetry. The values of SpO2 and maximum HR are recorded. The CLE is concluded when the patients are in a state of exhaustion or exhibit respiratory symptoms that preclude the continuation of the test.

CLE Assessment

All video recordings are reviewed after the completion of the CLE, and the movements at the glottic and supraglottic levels are evaluated at rest, with moderate effort, and with maximum effort during each phase of the respiratory cycle. At these levels, the degree of obstruction is classified from 0 to 3, with grade 0 indicating no obstruction and grade 3 indicating complete obstruction, according to the classification proposed by Maat et al.[9]. The next step involves the calculation of the sum (E) of the scores for glottic level obstruction with moderate effort (A), supraglottic level obstruction with moderate effort (B), glottic level obstruction with maximum effort (C), and supraglottic level obstruction with maximum effort (D). The diagnosis of EILO is confirmed when the sum (E) of (A)+(B)+(C)+(D) equals or exceeds 3[9]. The onset time of EILO was assessed, with the onset being considered rapid if the obstruction occurs from one respiratory cycle to the next, or slow if it occurs after several respiratory cycles. The resolution time of EILO following cessation of exercise exposure was also evaluated, with the resolution being considered rapid if the obstruction resolves in less than 5 minutes, or slow if it takes more than 5 minutes. The duration of the modified Bruce protocol was also documented, that is, the time to exhaustion.

During the implementation of our protocol, all individuals were able to sustain the exercise until they reached VO2 max or exhaustion. The endoscopic and spirometric parameters set forth in the protocol were successfully obtained from all the included patients without any technical compromises. All individuals were found to have normal laryngeal anatomy and exhibited normal laryngeal movement at rest prior to exercise. The protocol was initially applied to 10 healthy volunteers, with no subsequent changes during CLE. Currently, it is being used in clinical practice for selected patients with symptoms suggestive of EILO.

Discussion

CLE associated with the visual scoring system was proposed by Maat et al.[9] and is currently the gold standard for the diagnosis of EILO. CLE at CHULC is conducted in the spirometry laboratory, and the protocol has been adapted to the resources of Portuguese hospital centers from other international protocols. To date, it has been well tolerated by patients. In this protocol, patients scheduled for CLE are initially seen in an outpatient laryngology clinic for the collection of medical history and a physical examination with resting nasofibrolaryngoscopy. Patients are advised to discontinue their standard asthma and allergic rhinitis therapy 24 hours prior to the CLE. No patient undergoes the examination within two weeks following a respiratory tract infection. The current method enables a continuous and dynamic assessment of the laryngeal structures in each phase of the respiratory cycle, correlating it with an objective measurement of exercise intensity. The primary challenge in conducting the CLE lies in the requirement to achieve maximal effort testing[4]. According to Tervonen et al.[10], the use of a stationary bicycle is insufficient to replicate the symptoms of patients in 50% of the cases. Røksund et al. arrived at similar conclusions in their population study[16]. However, Mirza et al. reported that endoscopic visualization of the larynx during cycling exercise is superior to that during treadmill running, as patients keep the upper body stationary during the exercise, providing a more stable video recording[20]. Furthermore, this setup allows examiners to adjust the position of the laryngoscope during the test, which is not feasible during CLE on the treadmill without interrupting the assessment. However, it has been suggested that CLE should be conducted in accordance with the specific sport practiced by the patient, if they are an athlete[20]. Consequently, there has been an effort to develop CLE with alternative forms of exercise, specifically swimming[26]. Given the available resources and need for exam reproducibility, the CHULC protocol employs the treadmill as the exercise source.

The main strengths of this literature review are the substantial patient cohort included and the quality of the selected protocols, featuring a comprehensive analysis of multiple parameters. However, there are some limitations to consider, particularly the fact that three of the studies were retrospective cohorts and thus dependent on the quality of the collected clinical records. Case-control studies and case series are also methodologically less comprehensive. Subsequently, the population analyzed in each study is heterogeneous, and the protocols do not reflect the individual characteristics of the patients, particularly the differences in their usual physical exercise routines, thus failing to distinguish between athletes and sedentary individuals. There were also no comparative studies between different age groups or those that take into account the pre-existing comorbidities. Thirdly, the majority of the studies reported outcomes from a single pediatric center, which may impact the generalizability of the collected information due to the significant variability in human and material resources across different centers. It should also be noted that none of the included studies specify whether the diagnosis of EILO was due to isolated supraglottic obstruction, isolated glottic obstruction, or both, and the potential pathophysiological and clinical differences associated with each. Importantly, the majority of the studies refer solely to the Scandinavian population. Future studies that reflect the reality of the Portuguese population are necessary, as the prevalence of EILO in Portugal is still unknown. Furthermore, the criteria for referring a patient for CLE are not fully established yet. Additionally, there is a need to study the reproducibility of the test among peers, as well as the effect of the inherent learning curve. There are no studies that address the relationship between CLE positivity and the type of exercise performed or the associated atmospheric conditions, such as air temperature or humidity.

Conclusion

Based on the information gathered in the literature review, a protocol for performing CLE was developed, and its feasibility and suitability for application in a Portuguese institution were demonstrated using healthy volunteers. Further studies on patients with EILO are required to validate these findings.

Conflicts of Interest

The authors declare that there is no conflict of interests regarding the publication of this paper.

Data Confidentiality

The authors declare having followed the protocols in use at their working center regarding patients' data publication.

Protection of humans and animals

The authors declare that the procedures were followed according to the regulations established by the Clinical Research and Ethics Committee and to the 2013 Helsinki Declaration of the World Medical Association.

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Availability of scientific data

There are no datasets available, publicly related to this work.

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