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Feasibility and Tolerability of Measuring Translaryngeal Pressure During Exercise

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Objectives/Hypothesis: To determine if simultaneous tracheal and supraglottic pressure measurement performed during a continuous laryngoscopy exercise (CLE) test is possible, tolerable, and feasible, and if so, whether measurements can be used to determined airflow resistance over the larynx, thus providing an objective outcome measure for the CLE test, the gold standard for diagnosing exercise-induced laryngeal obstruction.

Study Design: Explorative descriptive clinical study.

Methods: A CLE test was performed with the addition of two pressure sensors (Mikro-Cath 825-0101; Millar, Houston, TX) placed at the epiglottic tip and at the fifth tracheal ring. To place sensors, laryngeal anesthesia and a channel scope were required. Tolerability and feasibility was determined by a Likert score and subjective indication from subjects and operators. Adjustments to the technique were made to increase tolerability. The pressure data were continuously collected and analyzed for artifacts, drifts, frequency response, and used with flow data to calculate translaryngeal resistance.

Results: All subjects (n = 7) completed all procedures. Two main areas of concern were identified regarding tolerability: application of topical anesthesia to the larynx and nasal discomfort due to the added diameter of the laryngoscope. Protocol adjustments improved both. Pressure data were obtained from all procedures in all subjects, were consistent, and followed physiological trends.

Conclusions: Continuous measurement of the translaryngeal pressure gradient during a CLE test is possible, feasible, and tolerable. A CLE test with direct measurement of the translaryngeal pressure gradient might become a valuable tool in the objective assessment of respiratory function, and normal values should be established in health and disease.

Key Words: Translaryngeal resistance, exercise test, exercise-induced laryngeal obstruction, exertional dyspnea.

Level of Evidence: NA

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INTRODUCTION

Exercise-induced dyspnea is a common patient complaint. Symptoms are sometimes due to poorly controlled asthma and arise from obstruction of the intrathoracic airways, a condition labelled exercise-induced bronchoconstriction (EIB).[1] Alternatively, symptoms may arise from obstructions of extrathoracic airways, most often involving the laryngeal structures and if so labelled exercise-induced laryngeal obstruction (EILO).[2] Despite EILO being a common disease, with a prevalence of 5% to 7% in the general adolescent population,[3,4] and as high as one in three in predisposed groups,[5,6] our understanding of the role played by the larynx during exercise in health and disease is at an early stage, with large knowledge gaps.

Airway scientists have recently agreed on a standardized way to establish an EILO diagnosis, based on visual images obtained from continuous laryngoscopy performed during ongoing exercise (continuous laryngoscopy exercise [CLE] test).[7,8] Grading systems are based on relative changes in laryngeal aperture size from rest to peak exertion during the CLE test. These verified grading systems all involve subjective decision making, and their reproducibility has been questioned.[9] Objective outcome measures are needed to disentangle diagnostic confusions between EILO, EIB, and asthma,[10,11] and to improve clinical decision making in relation to treatment of EILO, especially for cases where irreversible surgery is being considered.

Upper respiratory tract obstruction is also a common problem in exercising horses, causing poor performance and dyspnea as in humans, tracheal pressure readings

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being used to substantiate laryngoscopic observations.[12,13] In veterinary medicine, pressure readings have informed surgical decision making and provided objective outcome measures for research for decades.[14,15]

We hypothesized that measuring airway pressures during exercise in humans will inform our understanding of upper airway mechanics, clinical decision making, and provide an objective outcome measure. Pressure measurements in the upper airway have only been made in humans at rest.[16] The aim of this study was therefore to address if tracheal pressure measurement performed during a CLE test is possible, feasible, and tolerable, and if it can be used to determine airflow resistance over the larynx in exercising humans.

MATERIALS AND METHODS

Study Design and Subjects

We performed an explorative, descriptive clinical study to develop a feasible and tolerable test protocol for measuring translaryngeal pressure gradients in exercising humans. Test subjects (n = 7) were recruited from the pediatric and ear, nose, and throat departments staff of Haukeland University Hospital, Bergen, Norway, completing 11 CLE tests. Participants had unknown EILO status, but all were familiar with the CLE test. No subject was examined within 2 weeks of a respiratory tract infection. A general physical examination, including height and weight, was performed.

The study was approved by the Regional Committee on Medical Research Ethics of the Western Norway Health Region Authority (2017/636/REK vest).

Lung Function Measurements

Baseline lung function parameters were determined by a spirometer (JAEGER Vyntus; CareFusion, Höchberg, Germany) in accordance with guidelines of the European Respiratory Society,[17] recording forced vital capacity and forced expiratory volume in the first second.

Preparations for Pressure Recordings and CLE Test Protocol

A 12-lead portable electrocardiograph device was attached to the subject. Nostrils and nasal cavity were anesthetized with 4% lidocaine. An endoscopic video camera system (Visera, CLV-S40; Olympus, Tokyo, Japan) was connected to a fiberoptic laryngoscope (ENF-V2; Olympus) in a sterile plastic cover with work channel, which was advanced through a hole in a modified facemask (Hans Rudolph, Inc., Kansas City, MO) through the nasal cavity to the oropharynx. Lidocaine (4%) was used to anesthetize the vocal folds and proximal trachea by a dripping technique through the work channel. The laryngoscope was fixed to the headset. Two pressure sensors (Mikro-Cath 825-0101; Milar, Houston, TX) were introduced through the work channel. The first was positioned approximately at the first tracheal ring. The second was positioned at the epiglottis tip. The sensors were secured to the headset and connected to a data-acquisition box (Powerbox 8/35; ADInstruments, Oxford, United Kingdom), and data were collected and stored on a MacBook Pro laptop (Apple Inc., Cupertino, CA) using LabChart 8.0 software (ADInstruments). Data acquisition was set at 40 Hz. A video camera and microphone were placed in front of the subject to document external images and sounds, and the ergospirometry unit was attached to the facemask.

The Maximum Voluntary Ventilation Maneuver and the CLE Test

The CLE test, including spirometry and maximum voluntary ventilation (MMV) procedure, were performed as described previously,[8] with the pressure transducers as an added element. Gas exchange parameters were recorded using the breath-by-breath method. Subjects ran on a treadmill (Ergo ELG70; Woodway, Weil am Rhein, Germany), to individual experience of exhaustion using a modified Bruce protocol with 90-second incremental intensity steps. Gas exchange variables were recorded (JAEGER CPX; Vyntus, Hochberg, Germany).

Collection of Pressure Data and Calculation of Translaryngeal Resistance

Pressures were continuously measured. Pressure traces were visually evaluated for evidence of interference. Maximum inspiratory translaryngeal resistance was determined during the MVV maneuver, walk-to-run transition, and at exhaustion (the last 10 seconds of CLE test). An average of 10 consecutive breaths at these time points were noted. Translaryngeal resistance was calculated by the following equation: $[R_L = P_T - P_E / AF]$ where R_L is laryngeal resistance (cm H_2O/Ls^{-1}), P_T is tracheal pressure reading (cm H_2O), P_E is epiglottic pressure reading (cm H_2O), and AF is airflow in Ls^{-1} as determined by minute ventilation divided by 60, then multiplied by inspiratory ratio. Data validation was addressed by assessing the relationships between pressure data curves and flow curves, artifacts, drifts, and frequency responses. Tolerability was determined by subjective reporting from subjects during and after the test, and by Likert score 1 to 5 (see Supporting Information, Appendix 1, in the online version of this article) and observation of the laryngeal mucosa posttesting for signs of irritation. Feasibility was determined by subjective reporting from the operators and time taken to perform the test compared to a standard CLE-test.

Revisions of the Test Setup

After four test subjects had been examined, the setup was adjusted. Two percent topical lidocaine was used to anesthetize the vocal fold area, administered via an Olympus spray-tip catheter (PW-6C-1; Olympus) producing a mist of lidocaine instead of droplets. One milliliter was sprayed as the test subjects expressed a long /e/ (closed vocal folds) and 1 mL with the vocal folds abducted. Further doses were given as required, judged by the test subject eliciting a glottic closing reflex or not when the sensors tip came into contact with the laryngeal inlet.

The original laryngoscope requiring use of a sterile plastic cover with work channel was exchanged for a laryngoscope with a built-in work channel (ENF P3; Olympus). Nasal spray (xylometazoline 0.5 mg/mL hydrochloride) was introduced to reduce nasal cavity edema, allowing easier insertion of the laryngoscope.

The tracheal pressure sensor was advanced to approximately the fifth tracheal ring, minimizing the risk of accidental displacement into a supraglottic position, and ensuring the sensor be placed below any laryngeal jet effect.

The first four test subjects then repeated the test protocol according to these adjustments, so that all seven test subjects performed their examinations according to this revised protocol.

RESULTS

Seven subjects (Table I) completed 11 tests, with four subjects running both the primary and revised protocols. Data were collected from all subjects in all tests;

TABLE I.
Demographics of the Test Subjects.

Subject No.	Age, yr	Sex	FEV_1	Previously Performed a Standard CLE Test
1	61	Male	4.24	Yes
2	58	Male	5.02	Yes
3	40	Female	3.17	Yes
4	43	Female	3.00	No
5	41	Male	4.62	No
6	59	Male	4.11	No
7	56	Male	4.00	Yes

CLE = continuous laryngoscopy exercise; FEV_1 = forced expiratory flow in first second.

however, three of the primary protocol tests had issues with pressure catheter positioning or test performance leading to unreliable data. Subjects 2 and 3 did not run to exhaustion, and thus their CLE test data (but not their pressure data per se) where unreliable. Subject 4's tracheal catheter came out of position during MVV, determined by the pressure data not being consistent with the catheter being in a tracheal position.

Tolerability

There were variations in reported degree of discomfort (Table II), with two main areas of concern: insertion of the laryngoscope with a plastic cover and application of topical lidocaine to the laryngeal aperture. The subjects' feedback from the first setup of tests (n = 4) informed protocol revisions, after which tolerability improved, and all test subjects completed all planned examinations thereafter. The listed protocol amendments improved the average total Likert scale score from 2.4 to 1.7. Nasal discomfort during insertion of the laryngoscope and application of topical lidocaine to the laryngeal aperture area nevertheless remained the main causes of discomfort. Greatest improvement to tolerability was made by misting the lidocaine through a spray catheter instead of dripping, reducing Likert scale scores by one point in all individuals. Changing from a scope with plastic cover to a scope with a built-in work channel improved the average Likert scale score by 0.75. Having the tracheal pressure sensor positioned at the fifth tracheal ring did not cause any more discomfort than having the sensor at the more rostral position.

TABLE II.
Subjective Discomfort While Performing the Test.

Subject No.	Protocol 1	Protocol 2
1	3/3/1	2/2/1
2	2/3/1	2/2/1
3	3/3/2	2/2/1
4	3/3/2	2/2/1

Likert scores (1 = no discomfort to 5 = intolerable) addressing subjective discomfort (only four subjects completed both the original and the revised protocols). The first number indicates insertion of scope; the second number the application of lidocaine to the laryngeal aperture; and the third number denotes running with the continuous laryngoscopy exercise test with sensors in situ.

Feasibility

Feasibility in terms of timing improved rapidly with team experience, and testing was running relatively smoothly after having tested six subjects. The additional time required compared to a standard CLE test was approximately 10 minutes and linked to topically anesthetizing the larynx and sensor placement. Pressure measuring equipment requires minimal additional setup. The test can be performed with one doctor and one assistant as is protocol for the CLE test today; however, involving a third person makes testing easier. Using a scope with a built-in work channel improved feasibility, as it was easier to maneuver the scope to the correct position for application of topical lidocaine and to guide correct placement of pressure sensors.

Validation

Data acquisition at 40 Hz produced pressure curves with minimal interference while ensuring maximum and minimum pressures were recorded (Fig. 1). Pressure readings became more negative during inspiration and more positive during expiration, as airflow volumes increased, closely following the flow curves. Pressure measurements obtained from the sensors placed at the epiglottic and tracheal regions were temporally aligned (Fig. 1). There was no sign of temperature drift or damping of the pressure curves. Pressure readings obtained throughout the exercise tests from two different days from the same test subject were similar (Fig. 2). Having the tracheal pressure sensor at the first tracheal ring made it vulnerable to supraglottic displacement, especially at high airflow volumes, and advancing the sensor to the fifth tracheal ring prevented this.

DISCUSSION

This study has demonstrated that translaryngeal pressure measurements can be obtained while performing a standard CLE test in motivated, well-informed adult individuals. Added nasal discomfort due to the larger laryngoscope and the anesthetizing procedure of the laryngeal aperture and upper tracheal area constituted the main tolerability concerns. Pressure measurements could reliably be recorded throughout the maximal exercise test when the tracheal sensor was positioned at the fifth tracheal ring. Readings corresponded well to changes seen in airflow and rate of breathing, with no signs of drift, damping, or interference at 40 Hz acquisition. No adverse events occurred, and all participants completed all procedures. Overall setup required only minor extra equipment and time to complete, as compared to a standard CLE test. We consider the described setup to be tolerable and feasible for research, but its reproducibility and validity needs to be confirmed in properly designed studies before it can be applied in a clinical context.

Tolerability and Feasibility

Tolerability was predominantly affected by the laryngoscope diameter causing nasal discomfort on

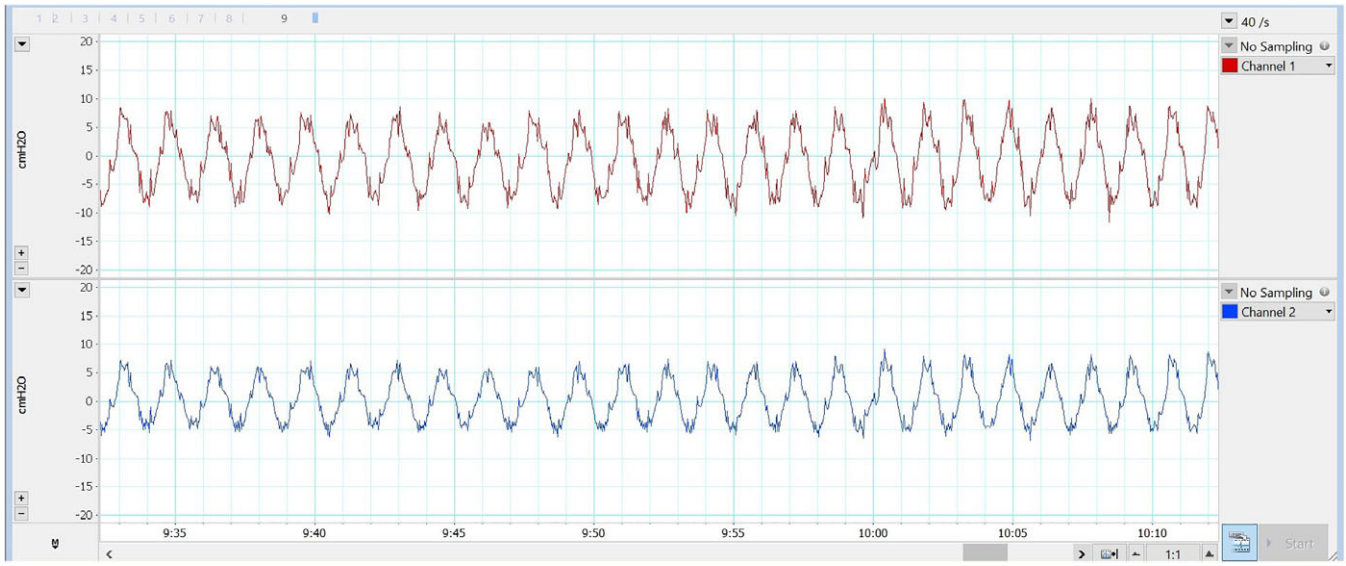

Fig. 1. Example of pressure tracing from the end of a continuous laryngoscopy exercise test, with the blue line depicting the epiglottic and the red line the tracheal pressure readings. At 40 Hz, maximum and minimum data are recorded, as seen by the even consecutive peaks. There is minimal background interference as seen by tracings with minimal secondary displacements. The epiglottic and tracheal tracings are temporally aligned, indicating that the tracings are well correlated. [Color figure can be viewed in the online issue, which is available at www.laryngoscope.com.]

insertion and by application of topical anesthesia to the laryngeal aperture. Modification to the original methodology improved tolerability of both concerns. Application of topical lidocaine to the laryngeal aperture was reported to be the most unpleasant part of the procedure by all participants. Altering the strength from 4% to 2% and misting as opposed to dripping improved tolerability. Further improvement may be achieved by a lidocaine nebulization, which has been extensively described in the literature for awake bronchoscopy and intubation.[18,19] Injection through the cricothyroid membrane is described for in-office laryngeal proceedures[20] and has been reported as providing better patient comfort than lidocaine nebulization for awake intubation.[21] Future testing will determine if these methods improve tolerability for tracheal pressure sensor placement without interfering with the very object of the procedure. A further benefit of the revised protocol was a more subject tailored approach with less lidocaine being used, leading to less stimulation of mucosal secretion, better visualization of the larynx, fewer swallow episodes and less subject discomfort.

A laryngoscope with a work channel reduces its diameter and facilitates introduction through the nasal cavity and improves control over the placing of the scope and the introduction of the sensors. However, the use of a channel scope increases both labor and costs, as cleaning between uses becomes significantly more laborious and costly than if using a scope in a protective sleeve. However, in most hospital environments the equipment and expertise needed to clean and store channel scopes is readily available.

Validity

40 Hz acquisition rate was chosen based on personal experience, published literature regarding equines, and resting pressure measurements in humans.[13,16] This acquisition rate ensured that maximum and minimum pressures were recorded, which may not have occurred at lower rates, while still keeping artifacts from probe movement and background noise at a low level. There was no evidence of damping by mucus or increasing humidity. The pressure traces obtained formed curves with consistent maximum and minimum readings over a period of unchanged breathing as would occur if only ventilation affected pressure. No drift from baseline with time suggests that significant temperature drift did not occur. The manufacturer (Millar Inc.) reports a $\pm$ 1 cm H_2O drift with temperatures between 25°C and 40°C, but such drifts did not occur here as airway temperature was relatively stable within the controlled laboratory environment and in the subjects' upper airways over the short testing time. Movement artifacts were minimal, and there were no obvious erroneous readings or outliers, except those that could be accounted for by speaking, coughing, and swallowing. This contrasts findings made at rest by Baier et al.,[16] who reported catheter whip, where the catheter made contact with the airway wall causing false pressure readings. Catheter whip may have been prevented in this study by the pressure sensors being supported in the work channel. In the Baier et al. study, the catheter was placed unsupported through the nostril opposite to the scope. In equines, whose airway pressures are much greater, the catheter is protected in a special plastic cover. Such protection was not deemed necessary in this study, as it seemed unlikely that the catheter would be exposed to the same magnitude of pressure change.

A concern with this methodology is that application of topical lidocaine might affect larynx function during exercise. Baier et al.[16] reported that topical lidocaine did not alter total respiratory system resistance. However, topical anesthesia of the equine airway has been reported to influence upper airway pressure measurements during exercise,

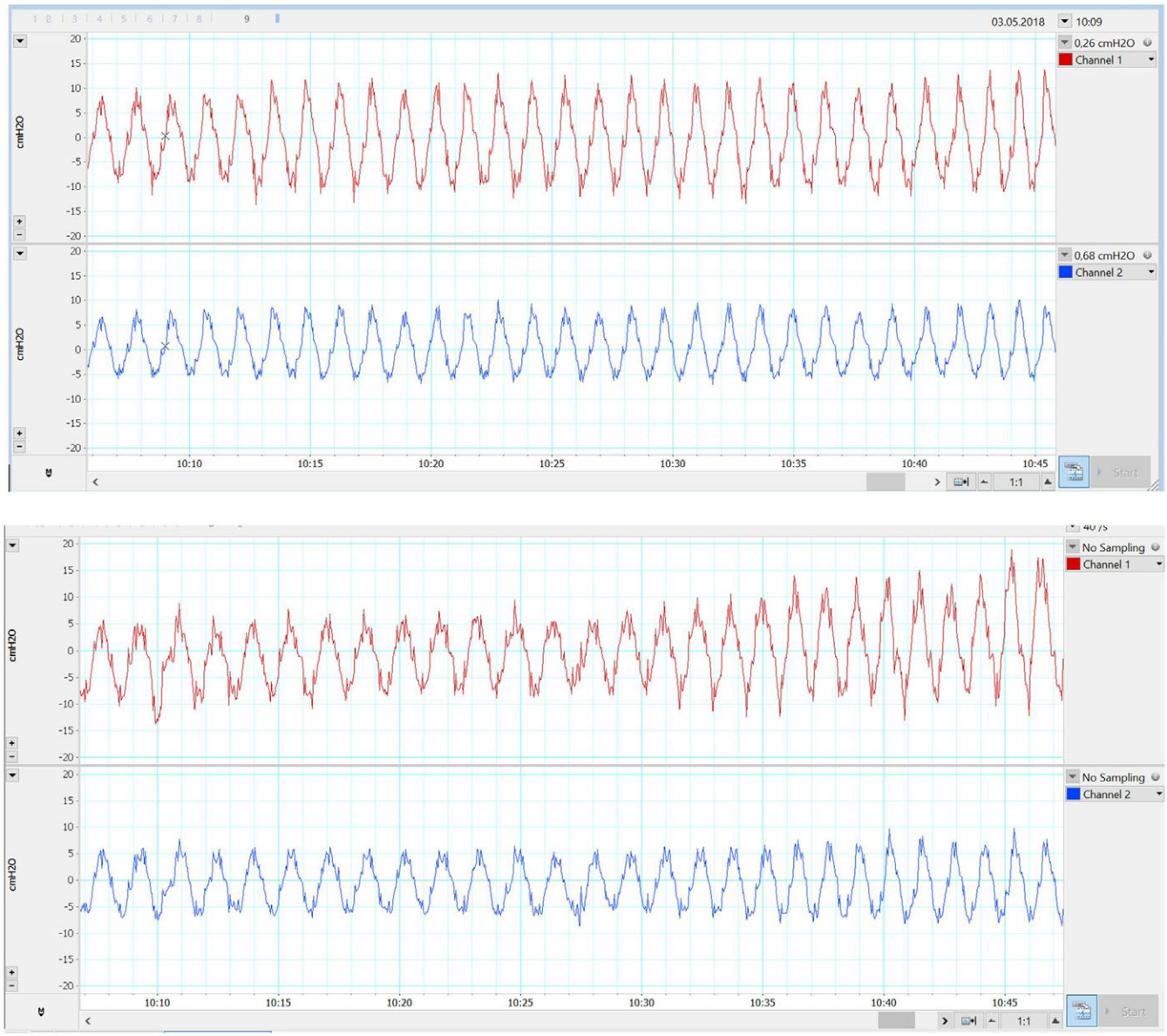

Fig. 2. Two separate tracings during the same time period from two different continuous laryngoscopy exercise tests, from the same individual, illustrating the similarities. The blue lines depict the epiglottic and the red lines the tracheal pressure readings. [Color figure can be viewed in the online issue, which is available at www.laryngoscope.com.]

although predominantly in the pharyngeal region.[22] Considering the anatomical differences between the equine and human oropharynx, notably the relationship between the soft palate and the epiglottis, the pharyngeal region is less likely to play a significant role for human laryngeal resistance, although further research is needed to confirm this. Obviously, these issues need to be understood before the test can be applied in clinical and research contexts in relation to patients suffering from EILO.

Resistance Calculations

Previous research in exercising equines and in humans at rest has shown that pressure traces are relatively similar in all individuals. However, during this research, it became evident that this was not the case during exercise in these test subjects. Pressure patterns during MVV were relatively similar in most individuals, but during exercise different trace patterns where seen, likely reflecting different breathing strategies adopted by individuals to increase their minute ventilation. Some subjects preferentially increase tidal volume, whereas others increase breathing frequency. The time ratio of inspiration to expiration also varied. Variations in pressure patterns became more evident with increasing exercise intensity. This affects the resistance calculations, as the total minute ventilation was used to determine flow at any given time. If the individual uses a short time on inspiration at the expense of expiration, this will result in an increased flow rate during inspiration and thus a

higher translaryngeal resistance. The data from this and future studies will take into account and be analyzed with these parameters to give more accurate resistance calculations and determine how different breathing strategies affect airway mechanics. Resistance was greater at walk-to-run transition than at the end of the CLE test, when flow was greatest, in all but two subjects. This is most likely explained by the observation on laryngoscopy that healthy individuals do not fully abduct the arytenoids until they are at running speeds. The laryngeal inlet area is smaller at walk-to-run than at the end of the CLE test, resulting in the increased resistance measured. These responses need to be explored in detail and linked with clinical data and images in future studies. The magnitude of inter subject variability for translaryngeal resistance readings in this study seems reasonable and consistent with variability in total airway resistance in studies using esophageal sensors to determine pleural pressure.[23]

Utility

The need for an objective and absolute outcome measure for the CLE test has been highlighted as a major research priority in recent European Respiratory Society/European Laryngological Society/American College of Chest Physicians statements.[2,7] Currently, only relative, subjective grading scales of laryngeal aperture size during increasing exercise intensity are available. This is an unsatisfactory measure particularly for irreversible clinical decision making (surgery) and research. This article describes a method for objectively assessing the resistance to airflow over the larynx during maximal treadmill exercise, applied as an add-on option to a standard CLE test. The method opens for direct and real-time comparisons between translaryngeal pressure drops obtained before and after treatments, and also as a comparison with visual changes of the laryngeal aperture as observed during a CLE test. The method also enables real-time translaryngeal resistance measurements in direct conjunction with observations of the patients' symptoms and with their cardiorespiratory parameters, as these variables are obtained throughout a CLE test.

CONCLUSION

Translaryngeal resistance measurements can be done in exercising humans, and thus hold potential to provide objective, continuous, numerical and verifiable data to describe laryngeal function during exercise. The method appears feasible and tolerable and provides reliable translaryngeal pressure measurements. If the larynx is viewed as the entrance valve to the airway tree, future access to such data can become as important to respiratory medicine as transvalvular pressure gradients are in today's cardiology.

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