



Measuring Inhalational Glottal Opening to Evaluate Surgical Outcomes in Adult-onset Laryngomalacia: A Novel Method for a Rare Entity

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Abstract

Introduction: Laryngomalacia (LM) is supraglottic collapse on inspiration, causing temporary airway obstruction. Congenital laryngomalacia is a well-described primary disorder in infants. However, adult-onset LM is rarely discussed in the literature. Adult LM can be acquired iatrogenically *via* trauma or neurodegenerative disease, or it may manifest as paradoxical vocal fold motion, methacholine-resistant asthma, or obstructive sleep apnea. We present the largest cohort of single institution adult-onset LM.

Methods: Patients were selected for retrospective review using the Voice Swallowing, and Airway database at the University of Cincinnati over a two-year period (March 2016 to May 2018). Charts were reviewed for patient characteristics, medical comorbidities, chief complaint, pulmonary function testing, polysomnography testing, and patient rated Dyspnea Index (DI). Inhalation images were reviewed and selected from recorded endoscopic exams by senior author (RH). Matlab[®] program was used to compute glottal opening Area (A) and Length (L) from manually delineating opening contours. A/L^2 was considered for each image as a non-dimensional comparison value between pre- and post-operative inhalational endoscopies.

Results: The study included 19 patients: mean age 49.4 years (range 16-97), 63% were female and 53% (BMI>30) considered obese. Sixteen (84%) presented with dyspnea and 10 (53%) with cough. Patients were categorized into acquired (n=14) and iatrogenic (n=5). Eleven patients underwent surgery (arytenoidectomy, supraglottoplasty, with/without staging) with an improvement in DI by 7.6 (SD=5.8). 90% of patient's demonstrated increased postoperative inhalation glottal opening A/L^2 compared to pre-operative value.

Conclusion: Adult-onset LM should be considered in patients presenting with dyspnea, cough or OSA like symptoms. We describe the use of inhalational glottal opening as a novel measure to describe pre-and post-operative LM surgical outcomes.

Keywords: Laryngomalacia; Supraglottoplasty; Obstructive sleep apnea; Inhalational glottal opening

Introduction

Laryngomalacia (LM) is defined as supraglottic collapse on inspiration leading to temporary airway obstruction and a spectrum of symptomatology for patients [1]. Adaptation during increased inspiratory effort (for example, exercise) in a normal larynx should be fixed abduction of the aryepiglottic folds and vocal folds, thereby increasing laryngeal aperture and decreasing resistance to airflow [2].

Laryngomalacia is most commonly associated with the pediatric population, and is the most common cause of inspiratory stridor in infants children typically present with stridor that worsens with feeding or sleep, and can also present with wheezing, respiratory distress and/or dyspnea [3]. Congenital presentation, repair techniques and etiologies are well described in the literature. It is diagnosed by laryngoscopy and typical regression is seen by 18 months to 24 months [4]. Laryngomalacia has also been associated with Gastroesophageal Reflux Disease (GERD) in children

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Received Date: 20 Sep 2019

Accepted Date: 15 Oct 2019

Published Date: 21 Oct 2019

Citation:

Harvey EA, De Luzan CF, Sarber KM, Khosla S, Howell RJ. Measuring Inhalational Glottal Opening to Evaluate Surgical Outcomes in Adult-onset Laryngomalacia: A Novel Method for a Rare Entity. *Am J Otolaryngol Head Neck Surg.* 2019; 2(9): 1073.

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Table 1: Patient characteristics and comorbidities.

	Sex (age)	Etiology	Presenting Complaint	Comorbidities of Interest
Patient 1	F (33)	Unilateral true vocal fold paralysis 2/2 papillary thyroid carcinoma, invasion into trachea and esophagus, 2 episodes of prolonged laryngitis	DOE, Fatigue	Thyroid disease, GERD, Obesity
Patient 2	M (61)	Unknown	Dysphagia, cough	Asthma, OSA without CPAP use, HTN, GERD, Obesity, Nasal spray use
Patient 3	M (55)	Unknown	Dysphagia, globus sensation	OSA, without CPAP use, HTN, Obesity, Nasal spray use
Patient 4	M (22)	Unilateral Vocal fold paralysis 2/2 multiple intubations	DOE, voice changes	Asthma with inhaler use, hx of multiple intubations (>20), OSA on CPAP, HTN, Seasonal Allergies, GERD, Obesity
Patient 5	F (55)	Unknown	Cough, DOE, Laryngospasm, voice changes, dysphagia	OSA on CPAP, HTN, Seasonal allergies, Thyroid multinodular goiter with compressive symptoms, GERD, Obesity, Nasal spray use
Patient 6	M (46)	Unilateral vocal fold paralysis 2/2 ACDF	DOE	HTN, GERD
Patient 7	F (97)	Unknown	DOE, Voice changes	NA
Patient 8	F (68)	Unilateral vocal fold paralysis 2/2 thyroidectomy	DOE	Thyroid disease, GERD
Patient 9	F (16)	Unknown	DOE, cough, Laryngospasm	Using inhalers, Seasonal allergies, Nasal spray use
Patient 10	M (33)	Mining explosion, inhalation injury and multiple intubations	DOE, cough, orthopnea	COPD (treated), HTN, Seasonal allergies, GERD, Nasal spray use
Patient 11	F (45)	Unknown	DOE, orthopnea	Seasonal allergies, thyroid disease, GERD, Nasal spray use
Patient 12	F (51)	Unknown	DOE, cough, fatigue	Asthma (treated), OSA not using CPAP, HTN, Obesity, Nasal spray use
Patient 13	M (56)	Unknown	DOE, Voice changes, Fatigue	Hx of multiple intubations, OSA not using CPAP, HTN, GERD, obesity, DM, Sarcoidosis
Patient 14	M (42)	Unknown	DOE, cough, orthopnea, voice changes	HTN, GERD Obesity, DM
Patient 15	F (24)	Unknown	DOE, cough, Voice changes	Seasonal allergies, Nasal spray use, Mild reactive airway with methacholine challenge, diagnosed asthma
Patient 16	F (53)	Unknown	DOE, voice changes, fatigue	HTN, Seasonal allergies, Thyroid disease, GERD, Nasal spray use, OSA
Patient 17	M (75)	Unknown	DOE, cough, voice changes, dysphagia	OSA on BiPaP, HTN, Obesity, DM
Patient 18	F(64)	Previous thyroidectomy	Cough, globus sensation	Thyroid goiter GERD, nasal spray use
Patient 19	F (43)	Unknown	DOE, cough, orthopnea, dysphagia, laryngospasm	Asthma (treated), HTN, Seasonal allergies, GERD, Obesity, Nasal spray use

A: Acquired group; I: Iatrogenic group; HTN: Hypertension; GERD: Gastroesophageal Reflux Disease; OSA: Obstructive Sleep Apnea; COPD: Chronic Obstructive Pulmonary Disease; M: Male, F: Female; ACDF: Anterior Cervical Discectomy and Fusion; DOE: Dyspnea on Exertion

[5].

Adult-onset LM is defined as patients with no prior history of LM that present with symptoms of supraglottic collapse. Entirely adult-onset LM is considered rare in the literature, but may be more common than once thought. Etiology in adults is reported as acquired or idiopathic. Most common categories of related etiology include: Iatrogenic (secondary to multiple intubations and surgery), neurologic insult and thyroid disease [6]. Diagnosis is confirmed by awake fiberoptic laryngoscopy with visualization of inward collapse on inspiration.

The purpose of this paper is to summarize demographics of patients diagnosed with adult-onset laryngomalacia in order to categorize those patients into acquired or idiopathic subgroups and describe the management of LM. We hypothesized that surgical intervention (supraglottoplasty, partial arytenoidectomy) would improve symptomatic dyspnea (using the Dyspnea Index) and improve inhalational glottal opening (a novel tool described herein).

Methods

Study subjects

Patients diagnosed with adult-onset laryngomalacia (by senior

authors RH, SK) were selected for retrospective analysis using the Voice, Swallowing, and Airway database at the University of Cincinnati from March 2016 through May 2018. Charts were reviewed for age, gender, Body Mass Index (BMI), medical comorbidities, chief complaint, Pulmonary Function Testing (PFTs), Polysomnography (PSG) results, and patient rated Dyspnea Index (DI) [7]. Obesity was defined as BMI>30 kg/m². Subjective complaints were collected from the first clinical visit (Table 1).

Surgical intervention

Surgical categories were divided into: partial arytenoidectomy (removal of redundant mucosa with or without the corniculate cartilage) and supraglottoplasty (incision of the aryepiglottic folds and redundant supraglottic tissue). Additional procedures at the time of intervention were also recorded, and revision rate was documented (Table 2).

Dyspnea Index (DI)

Patients were provided a validated 10 questions DI questionnaire at each clinic visit. These values were collected in chart review or as part of the Voice, Swallowing and Airway database. Patients score from 0, indicating never having symptoms to 4, indicating always symptomatic. Ten symptoms or scenarios are assessed, totaling up to

Table 2: Interventions provided for patients with adult-onset LM divided by etiology.

	Acquired (n=14)	Iatrogenic (n=5)
Underwent Surgical Intervention	9	4
Arytenoidectomy	5 (bilateral)	2 (unilateral)
	3 (unilateral)	
Supraglottoplasty	5 (bilateral)	2
	1 (unilateral)	
Additional procedures	3 (bilateral fat injection, unilateral fat injection, esophagoscopy with dilation)	2 (fat injection)
Revision	2	1
Voice Therapy†	4	0

†: Performed by speech language pathologist at same or subsequent visits

Table 3: Baseline polysomnographic values for patients with obstructive sleep apnea.

Patient#	Apnea-hypopnea index (events/hour)	Oxyhemoglobin nadir (%)	Percentage of total sleep time in REM (%)
Patient 5	10.1	74	55
Patient 12	19.2	84	11.8
Patient 13	96†	52	N/A
Patient 17	87.7†	60	N/A

†: Results of home sleep apnea test; REM: Rapid Eye Movement stage of sleep, N/A: Data Not Available

40 for the index score.

Area of inhalation

We acquired stroboscopy video for each patient, from which we extracted a pair of images, one prior to surgery and at least 3 months after surgical intervention. Through the video stroboscopy, a still image was selected by senior author (RH) to best represent an inhalation. For each image pair, we computed the glottal opening Area (A) and Length (L) using a triangulation script, run in Matlab. The area was obtained by manually delineating the opening contours with a computer mouse (Figure 1a and 1b). The script then used the defined points to triangulate the enclosed area and calculates its value in pixel [2]. The length is obtained by selecting the membranous vocal fold most visible on the still image and recorded its length as the vocal process to the commissure (Figure 2a and 2b). In order to obtain a non-dimensional number for comparison between different stroboscopes, the ratio A/L^2 was considered for each image. It is representative of the shape factor of the glottal opening, while being independent of the scaling of the images, which is different in each case due to arbitrary scope position and subsequent camera angle relative to the vocal folds. A slot-like elongated glottal opening will yield $A/L^2 < 1$ while $A/L^2 \sim 1$ will correspond to a wider opening along the medial direction, diamond shaped opening. We compared the ratios of the image after surgery (A/L^2) post to the preoperative image (A/L^2) pre in order to determine what effect surgery had on the shape of the glottal opening.

Statistical analysis

Statistical evaluations were performed using R Foundation for Statistical Computing, Vienna, Austria (<https://www.R-project.org/>). Mean and standard deviation were used to describe parametric continuous variables, while median and range were used for non-parametric variables. For paired data before and after intervention, a Wilcoxon signed-rank test was used to assess significance and the median difference between before and after values was reported.

Results

Patient demographics

Nineteen patients with a mean age of 49.4 years (range 16-97)

were identified. 63.1% (n=12) of patients were female. Mean BMI was 34.0 kg/m² (standard deviation SD 9.5). Comorbid medical issues of interest included: Hypertension (HTN) (n=12), seasonal allergies (n=8), thyroid disease (n=7), smoking (n=0), GERD (n=13), obesity (n=10), Diabetes Mellitus (DM) (n=4) (Table 1). The most common chief complaint was dyspnea on exertion (84%, n=16), followed by cough (53%, n=10), orthopnea (21%, n=4), voice changes (42%, n=8), dysphagia (21%, n=4), and fatigue (16%, n=3). Concomitant medical issues and previous diagnoses included 21% (n=4) with asthma, 5% (n=1) with COPD. Five patients (26%) of patients were prescribed and actively using inhalers or bronchodilators. Two patients (10%) had prior history of multiple intubations. Seven (36%) patient had been diagnosed with Obstructive Sleep Apnea (OSA); of those, 4 had a PSG available for review. Only 2 patients were regularly using positive airway pressure.

Based on history and etiology of LM, patients were divided into two groups: acquired (73.6%, n=14) and iatrogenic (26.3%, n=5). The acquired group included patients with methacholine resistant asthma (n=2), OSA (n=4) and idiopathic (n=8). The iatrogenic group included patients with multiple intubations (n=1), inhalational injury secondary to a mining accident (n=1), and unilateral vocal fold paralysis (n=3).

Surgical intervention

Thirteen patients (68.4%) underwent surgical intervention. Four patients received Respiratory Re-training therapy with a Speech Language Pathologist (Table 1).

Dyspnea index

Pre-intervention DI was available for 10 of the 13 patients who received surgery. The mean DI was 21.1 (SD 9.2). Post-intervention (at least 3 month follow up) DI was available in 7 of 13 patients. There was a significant change in DI scores between pre-operative and post-operative DI (median change =6, p<0.02) (Figure 3).

Change in area

Ten out of 13 patients had valid video stroboscopy images pre and post operatively. Change in area (Post (A/L^2)/Pre (A/L^2)) was

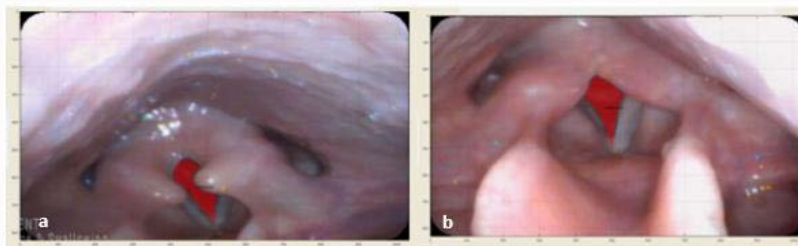


Figure 1: a) Pre-operative manual area delineation using the triangulation script. The red shaded area indicates the manually selected area of glottal opening during inspiration. b) Post-operative manual area delineation using the triangulation script. The red shaded area indicates the manually selected area of glottal opening during inspiration.

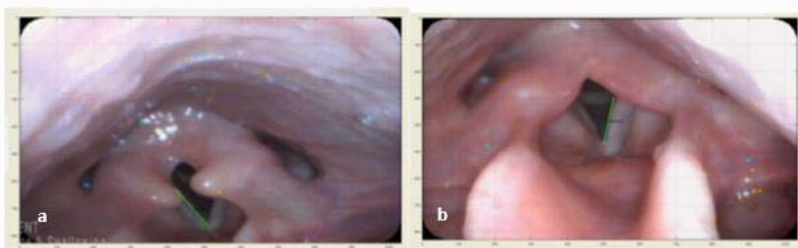


Figure 2: a) Pre-operative manual length of the membranous vocal fold, shown in green. b) Post-operative manual length of the membranous vocal fold, shown in green.

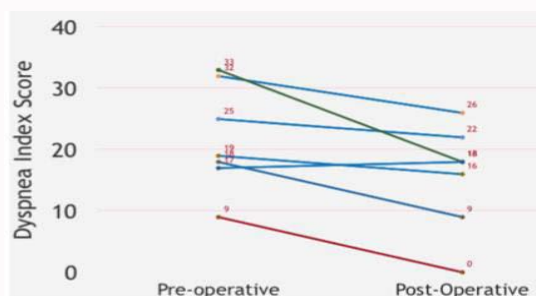


Figure 3: Patient reported outcome Dyspnea Index (DI) pre and post operatively.

greater than 1.0 (indicating improved postsurgical change) in 8/10 of these patients (Figure 4).

Obstructive sleep apnea

Seven patients (37%) had comorbid obstructive sleep apnea. Four patients had polysomnographic data available for review. Mean AHI was 53.3 events/hour (range 10.1 to 96). Mean oxyhemoglobin nadir was 67.4% (range 52 to 84). Postoperative PSG data was not available for any patients. PSG data for these patients is seen in Table 3.

Discussion

Review of literature

Pediatric LM is clearly defined, whereas the adult-onset LM may be less appreciated but perhaps more common than we think. Assessment of tissue redundancy and subjective symptoms guide the treatment course. Etiology of this pathology has not been well described in the literature but is typically attributed to either idiopathic or acquired. LM has been described as impairment of motor tone of the larynx following neurological insult, idiopathic due to resection of oral cancer or other thyroid surgery, laryngeal fracture, or potentially exercise induced [1,8]. Exercise Induced Laryngomalacia (EILO), initially reported in 1995 by Smith et al. [9]

is seen commonly in teenage female athletes. What we would consider an acquired etiology; the lumen for airflow has been hypothesized to be mechanical obstruction due to active muscle contraction at the epiglottic level due to increased Bernoulli forces during strenuous activity [2]. The idea that laryngomalacia could contribute to OSA has been explored in the literature, and redundant laryngeal tissue has recently been associated with OSA, GERD and obesity [10].

Follow up in this patient population is physician dependent but is typically done with video stroboscopy in the office and symptomatically. This is the first to describe DI as it pertains to this population.

Treatment of this patient population varies, but most includes a surgical approach. In the largest review of this patient population, the most common intervention was laser supraglottoplasty using CO₂ laser (31%), followed by epiglottectomy and finally tracheostomy [6,11].

Our outcomes

Our study is the largest single-center review of patients with surgically treated adult-onset laryngomalacia. We found that both the subjective measure of outcomes (DI) and objective measure of outcomes, inhalational glottal opening, improved after surgical intervention.

Subjective outcomes in patients with dyspnea related complaints are commonly assessed by dyspnea index. Dyspnea was the chief complaint among 86% patients; therefore, the DI may not be a reliable indicator of symptom improvement for the other 14% of patients. Furthermore, we did not assess other objective measures of dyspnea such as pulmonary function testing. We did use videolaryngoscopy to assess and evaluate treatment response.

Patients with improved pictures of inhalation pre and post operatively were noted. Although these values were not statistically assessed, they represent a novel way to objectively measure outcomes in these patients and other glottal expansion surgeries.

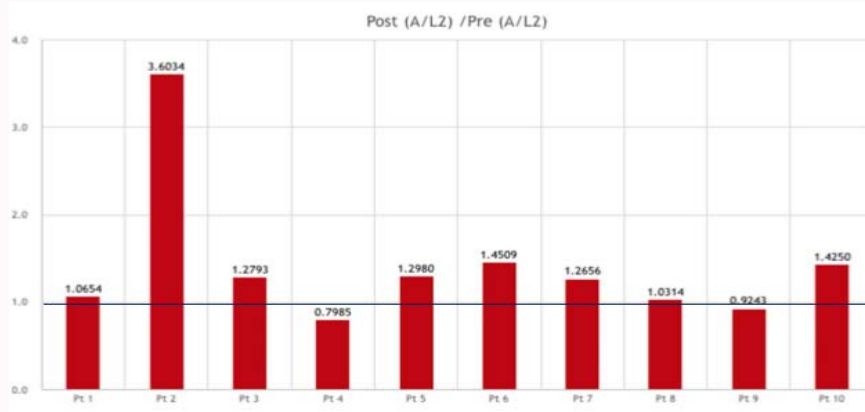


Figure 4: Area of inhalation compared pre and post-surgical intervention.

OSA and LM

In the pediatric population, LM is commonly associated with OSA in young children. LM has been shown to be present in 43.6% of patients with OSA that underwent bronchoscopy [12]. Conversely, for inpatient children with LM, the odds of undergoing a PSG during their hospital stay were 17 times more likely than children without LM [13]. Supraglottoplasty has been shown to improve the AHI and has been proven as valid treatment for this population [14,15].

A large percentage of our cohort had comorbid OSA, indicating a possible association between LM and OSA. Adult LM has been reported to be associated with obstructive sleep apnea in various case reports, series, and prospective studies [8,16-21]. Gillespie et al. [18] used pressure manometry during sleep to demonstrate that 2 patients with OSA and clinical laryngeal dysfunction showed collapse only at the larynx. This collapse was reversed with nasal CPAP. Kezirian et al. [17] reviewed drug induced sleep endoscopy in patients with OSA and showed that the epiglottis contributed to upper airway obstruction 29% to 30% of patients.

Only a few case series describing the surgical treatment of laryngeal obstruction report outcomes related to OSA. Woo et al. [8] presented 2 patients with witnessed apneas at night, daytime somnolence with exam showing epiglottal obstruction of laryngeal inlet on inspiration. After undergoing surgery, the patient had complete resolution of symptoms and on flexible laryngoscopic exam. Chetty et al. [16] presented 1 patient one patient with OSA four years after radical neck dissection and radiotherapy, found to have a large flaccid epiglottis, large aryepiglottic folds and edema of the supraglottic area on bronchoscopy. Golz et al. [21] looked at 27 adult patients who were diagnosed with OSA by PSG who underwent fiber optic laryngoscopy which indicated various degrees of laryngeal inlet obstruction either due to abnormal epiglottis or backward displacement of epiglottis on posterior pharyngeal wall using a standardized rating scale. Relief in snoring and daytime somnolence was seen in the majority of patients, and PSG data at least 1 year postoperatively showed a significant ($P < 0.01$) decrease in RDI in 21 patients. Yiu et al. [10], in describing the Shar Pei Larynx, described 22 patients with OSA as comorbidity. Twenty of these patients were previously diagnosed, and 2 were diagnosed as a result of Shar Pei Larynx findings. These patients were divided into severe, mild-moderate and unknown.

Limitations

Limitations of this study included retrospective nature, subjective

maximum inhalational opening performed by senior author (RH). There was no control group to compare outcomes due to the small patient population. Although dyspnea was the most common complaint, use of DI as a patient reported outcome has limited utility in a (likely) multifactorial disease.

Due to the incomplete PSG data, it is difficult to draw a clear correlation between LM and OSA. However, subjectively, patients reported improved snoring and better compliance with positive airway pressure after surgery.

Conclusion

Adult-onset laryngomalacia has a variety of etiologies and manifestations which can be difficult to categorize based on initial complaints and patient history alone. We would like to suggest including this diagnosis in the differential for patients presenting with dyspnea, worsening asthma not responsive to treatment and as a possible contributing factor to OSA. Dyspnea index and Inhalational glottal opening proved to be consistent markers for improvement in the Acquired patient population after surgical intervention. Inhalational glottal opening may be an outcomes measure for other supraglottic expansion surgeries. In the future, use of Pulmonary Function Testing (PFT) could give more insight into this patient population. Additionally, it will be important to obtain post-operative PSG to determine if surgery improves OSA. We recognize the need for long term follow up and routine otolaryngology visitation in this patient population.

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