Sleep-disordered breathing and laryngomalacia

An Boudewyns

Antwerp University Hospital, Department of Otorhinolaryngology, Head and Neck Surgery, Antwerp, Belgium
University of Antwerp, Faculty of Medicine and Translational Neurosciences, Antwerp, Belgium

an.boudewyns@uza.be

Keywords

obstructive apnea, central apnea, laryngomalacia, polysomnography, supraglottoplasty

Abstract

Congenital laryngomalacia, the most frequent cause of inspiratory stridor in infants, can be associated with sleep-disordered breathing. A high prevalence of obstructive sleep apnea (OSA) has been documented among infants with laryngomalacia and surgical treatment by supraglottoplasty improves OSA severity. Consequently, polysomnography plays a role in the diagnostic evaluation, therapeutic decision making and follow-up after treatment of congenital laryngomalacia. A subgroup also presents with central apneas but the effect of treatment on the central apneas is rarely reported. Sleep-dependent laryngomalacia may be the primary cause of OSA in a minority of children and is the 2nd most common cause of persistent OSA after adenotonsillectomy. Children with sleep-dependent laryngomalacia are typically older (> 2 years), present with OSA related symptoms but do not have an inspiratory stridor while awake. Sleep-dependent laryngomalacia can be readily diagnosed by sleep-endoscopy and responds to surgical intervention by supraglottoplasty.

1.Introduction

Laryngomalacia is the most common cause of congenital stridor and typically presents in infants during the first weeks of life. It is caused by a dynamic, inspiratory obstruction of the supraglottis, both during wakefulness and sleep. Supraglottic collapse during sleep may result in sleep-disordered breathing (SDB).

More recently a different clinical entity was described in children beyond the neonatal period (usually > 2 years old) in which a collapse of supraglottic structures is only observed during sleep. This phenomenon results in increased respiratory effort and airway obstruction during sleep and causes daytime symptoms of OSA but no stridor.

Various terms have been introduced to describe laryngomalacia that only presents during sleep: state dependent laryngomalacia, occult laryngomalacia, sleep exclusive laryngomalacia, late onset laryngomalacia, or sleep-dependent laryngomalacia (1-6). For the purpose of this paper, we will use the term sleep-dependent laryngomalacia.

In the following paragraphs, I will discuss the epidemiology, the pathophysiology, the association with sleep-disordered breathing and the effect of supraglottoplasty on sleep-disordered breathing for both congenital and sleep-dependent laryngomalacia.

2. Congenital laryngomalacia.

2.1 Classification of congenital laryngomalacia

In congenital laryngomalacia, upper airway obstruction is typically attributed to short aryepiglottic folds, inspiratory collapse of redundant supra-arytenoidal mucosa and/or a collapse of the epiglottis against the posterior pharyngeal wall. Different classification systems have been developed to describe the pattern of collapse. The classification system by Olney et al. is widely adopted in clinical practice and was found helpful to guide surgical treatment (7, 8). Video 1 provides an example of a type 1 and 2 laryngomalacia with short aryepiglottic folds and inspiratory prolapse of supra-arytenoidal mucosa blocking the laryngeal inlet.

Video 1: *Type 1 and type 2 laryngomalacia co-occurring in an infant presenting with inspiratory stridor and OSA*

2.2. Pathophysiology of congenital laryngomalacia

The pathophysiology of congenital laryngomalacia is not yet fully understood. The anatomical theory dates back to 1897 when Sutherland and Lack proposed that laryngomalacia results from a congenital malformed larynx with immaturity of the tissues – a so called infantile appearing epiglottis (9). However, histological proof of an abnormal laryngeal cartilage or soft tissue is lacking (10). In addition, the anatomical theory does not account for the varying degrees of symptoms among infants with laryngomalacia. Based upon extensive clinical research in infants with laryngomalacia of varying severity and a wide range of clinical presentation, D. Thompson formulated a neurological theory (11). According to this neurological theory, laryngomalacia is caused by an abnormal sensorimotor function of the larynx related to immaturity or abnormal integration of peripheral nerves such as the posterior laryngeal nerve, the brainstem nuclei and central pathways involved in maintenance of upper airway patency.

The neurological theory is in accordance with several clinical observations:

1) symptoms worsen during sleep in a subgroup of infants with laryngomalacia, causing obstructive sleep apnea;
2) maturation of the peripheral and central nervous system may explain a spontaneous resolution by age 2 in the majority of infants;
3) laryngomalacia may develop after a neurological insult;
4) outcomes of treatment are worse in children with underlying neurological conditions or comorbidities for whom a correction of the "anatomical" abnormality is insufficient.

2.3 Symptoms of congenital laryngomalacia

Inspiratory stridor, which starts within the first few days of life, is the main symptom in infants presenting with congenital stridor caused by laryngomalacia. Other symptoms may be present in varying degrees such as feeding difficulties, choking, apneas, regurgitation, cyanosis, weight loss. Children with moderate disease may present with inconsequential brief apneic episodes whereas those with severe disease may have life-threatening apneic episodes and consequences of obstructive breathing such as failure to thrive, pulmonary hypertension and cor pulmonale (11, 12).

2.4 Treatment of congenital laryngomalacia

Congenital laryngomalacia is commonly described as a condition that present shortly after birth, worsens in the first months of life, gradually improves thereafter

and resolves by age 18 months (11). As such, most patients can be managed with a non-surgical approach including feeding modification and treatment of gastro-esophageal reflux. It is widely accepted that about 10 to 20% of patients with congenital laryngomalacia would require surgical intervention because of severe symptoms (11).

Surgical intervention is advocated in children with feeding difficulties and failure to thrive, cor pumonale and episodes of cyanosis and apnea. Factors that are associated with an indication for surgery are prematurity, younger age at presentation and emergent evaluation in the hospital (13).

Endoscopic treatment of laryngomalacia by supraglottoplasty aims to trim the aryepiglottic folds, to remove redundant supra-arytenoidal mucosa and is the first line surgical treatment modality (6). Epiglottopexy is performed in cases of type 3 laryngomalacia with retroflexion of the epiglottis against the posterior pharyngeal wall completely covering the laryngeal inlet (14).

Tracheotomy is reserved for supraglottoplasty failures or infants with multiple comorbidities requiring tracheotomy for additional reasons other than airway obstruction (14).

Only few authors report on their experience with continuous positive airway pressure (CPAP) as a treatment modality for congenital laryngomalacia associated with obstructive sleep apnea (OSA). Zwacka et al reported on successful CPAP treatment in 10 infants with congenital laryngomalacia (15). Application of CPAP pressures between 4 and 7 mbar resulted in an immediate clinical improvement with a decrease of heart and breathing rate, an improvement in oxygen saturations and relief of inspiratory stridor. The effect of CPAP on the laryngeal appearance was documented by flexible endoscopy performed under chloral hydrate sedation.

In infants with laryngomalacia associated OSA that are deemed unfit for surgical intervention or when parents decline surgery, CPAP treatment may be considered a valuable non-invasive treatment option.

2.5 Sleep-disordered breathing and congenital laryngomalacia

Although apneas during sleep are recognized as a symptom of congenital laryngomalacia, only a few studies investigated the prevalence of SDB in children with congenital laryngomalacia.

Thanphaichitr et al. investigated the prevalence SDB in infants with congenital laryngomalacia (16). Data were available for 54 patients of whom 33.3% presented with an underlying neurologic disease, hypotonia or syndrome and 14,8% had a history of prematurity. A diagnosis of OSA (obstructive apnea/hypopnea index 1 event per hour) was made in 92.6%. Central sleep apnea syndrome (CSA), defined as central apnea index 5/h, was identified in 46.3%. Interestingly, 38.9% of children without risk factors had CSA. In a study by Fard et al, 108 patients had confirmed laryngomalacia and nearly half (52%) underwent a polysomnography (PSG) (17). Among them, 44 out of 56 (79%) were diagnosed with OSA. There were only 3 patients with a central apnea index (CAI) > 1/hour. Important to note is that this study included not only infants but also older children with sleep-dependent laryngomalacia. The mean age of the study population was 1.36 (0.65-3.18).

In a more recent study by Verkest et al. OSA, defined as obstructive apnea/hypopnea index 2/h, was diagnosed in 77% of the 44 patients with laryngomalacia. An elevated central apnea index 1/h, was found in 57% and 7 % had a CAI >5/h (18).

2.6 Value of polysomnography in the diagnostic approach to congenital laryngomalacia

The role of polysomnography in the diagnostic work-up for infants with congenital laryngomalacia is poorly defined. In a recent paper published by IPOG (International Pediatric Otorhinolaryngology Group) on diagnosis and management of laryngomalacia, PSG was considered and adjunct and the authors recommended oximetry or PSG in cases with significant apneas (12). The study by Verkest et al. illustrated the potential value of PSG in the decision - making process for infants with laryngomalacia. In this paper, the severity score of laryngomalacia was altered in nine patients from mild to moderate and in 13 from moderate to severe. Polysomnography was found to be a useful non-invasive tool in the assessment and follow-up of infants with laryngomalacia. However, treatment decisions should be based upon the whole clinical picture, PSG and endoscopic findings (18). This conclusion is also supported by Cortes et al. who investigated the presence of OSA and sleep disturbances in children with severe laryngomalacia and the effect of supraglottoplasty on PSG parameters (19). In this study 11 patients with severe laryngomalacia based upon clinical symptoms and confirmed by flexible or rigid endoscopy underwent a polysomnography. All patients were diagnosed with severe OSA. The authors considered PSG as a non-invasive tool to identify OSA in children with severe laryngomalacia and to support surgical decision making.

Tawfik and colleagues investigated trends in indications for polysomnography in a large tertiary care hospital over a nine year period (from 2003 till 2012). The frequency of laryngomalacia as an indication for PSG increased from 2.5% to 14.3% and this difference was statistically significant. The authors assumed that this would reflect the increasing awareness among clinicians on the high prevalence of sleep disorders among infants with laryngomalacia (20).

Whereas only a few studies investigated the prevalence of SDB in cases of congenital laryngomalacia, several studies investigated the effect of treatment on polysomnographic parameters. These studies documented an improvement in PSG parameters after supraglottoplasty and concluded that PSG is an effective method to assess the efficacy of supraglottoplasty (19, 21-23).

2.7 Natural history of congenital laryngomalacia.

Symptoms of congenital laryngomalacia and especially stridor and respiratory distress resolve by 12-18 months of age (24). The natural evolution of other clinical manifestations such as OSA and endoscopic findings of laryngomalacia is yet unclear. Fard et al. investigated whether there is a spontaneous improvement in those children presenting with laryngomalacia and OSA whose laryngomalacia improves spontaneously (17). In the report by Fard et al, 34 out of 44 children with OSA and laryngomalacia and a mean age of 1.9 years, did not undergo a surgical intervention (17). They had a mean apnea/hypopnea index (AHI) of 2.1/h, nine underwent repeat PSG with a mean AHI of 1.5/h. The authors suggested that OSA may resolve with spontaneously improving laryngomalacia but the exact resolution rate could not be extrapolated given the limited number of patients that underwent a repeat PSG.

Moreover, the recognition of so called laryngomalacia variants presenting primarily with sleep-disordered breathing or swallowing disfunction in children beyond 18 months has challenged the evidence that laryngomalacia is characterized by spontaneous resolution in a vast majority of the cases. Isaac et al performed a systematic review on the natural history of laryngomalacia in otherwise healthy newborns without comorbidities or secondary airway lesions. These authors concluded that there is limited, level IV evidence for a spontaneous resolution of stridor and respiratory distress but that other endpoints such as endoscopic resolution or resolution of OSA have not been studied (1).

3. Sleep-dependent laryngomalacia

3.1 Clinical findings in sleep-dependent laryngomalacia

As an introduction to sleep-dependent laryngomalacia, I will first present a clinical case.

A 14 month old boy was admitted at the pediatric ENT department upon referral by the pediatrician. Pregnancy and birth were unremarkable, but the parents noticed noisy breathing and snoring since birth. He sleeps restless and awakens four to five times each night. The parents also noticed apneas during sleep. There are no other health related issues, growth and weight gain are age appropriate. Flexible upper airway endoscopy at another hospital was reported as normal. At the age of eleven months, a polysomnography was performed and showed moderate OSA: OAHI 5.5/h, CAI 1.8/h, Mean oxygen saturation 96.8% and lowest oxygen saturation 90%. Video recording during PSG showed noisy breathing, no snoring and frequent coughing during the night. A direct laryngoscopy was performed at the age of 14 months under general anesthesia with spontaneous breathing. This examination showed mild adenoidhypertrophy (< 50% obstruction of the rhinopharynx)

and laryngomalacia with inspiratory collapse of redundant supra-arytenoidal mucosa. The endoscopic findings are illustrated in Video 2.

Video 2: *Sleep-dependent laryngomalacia in a 14 month old boy presenting with OSA*

In 1997, Amin and Isaacson were the first authors to describe a condition called state-dependent laryngomalacia (10). These authors published a series of five infants (seven weeks to eight months of age) who presented normal breathing during wakefulness but had stridor and increased respiratory effort during sleep (10). Flexible endoscopy under anesthesia revealed a diagnosis of laryngomalacia. Follow-up was conducted by telephone interview and a resolution was reported between 6 and 15 months of age. In 2005, Smith et al. described a series of four children, aged 3-4 years, presenting with a primary complaint of noisy breathing during sleep. A diagnosis of laryngomalacia was established through an endoscopic examination under general anesthesia. Because the findings of laryngomalacia were only present in a hypotonic neuromuscular state and not during wakefulness, the term state-dependent laryngomalacia was coined and a neuromuscular system immaturity or disfunction for observations was proposed.

In 2008, Richter et al defined sleep-dependent laryngomalacia as a clinical entity causing OSA in children beyond the neonatal period or first year of life (6). In line with earlier reports, the authors emphasized that these children do not present with inspiratory stridor but rather exhibit OSA related symptom such as snoring, restless sleep and apneas during sleep.

3.2 Pathophysiology of sleep-dependent laryngomalacia

The neurological theory of laryngomalacia could also explain sleep-dependent laryngomalacia, a condition only present during sleep when the neurological dysfunction is exacerbated by a reduction of neuromuscular tone which characterizes sleep onset. However, other factors such as gastro-esophageal reflux are thought to play a role (6). In addition, in cases where another obstructive lesion coexist with laryngomalacia, the malacia may be the result of a central mechanism affecting laryngeal muscle tone after a period of chronic hypoxia or CO_2 retention related to SDB (6, 25).

It is not yet fully elucidated whether sleep-dependent laryngomalacia represents a distinct clinical entity or rather a continuum of a disease process starting early on in life (1). Revell and Clarke hypothesized that some infants with laryngomalacia might never have been properly diagnosed. A delay in diagnosis may be related to several causes: atypical and non-alarming complaints, underreporting of symptoms by parents, insurance issues or limited access to medical care amongst others. Thevasagyam et al. found that, upon active inquiry, half of the children with late onset laryngomalacia had swallowing or airway problems during infancy (25). Under these conditions, laryngomalacia would represent a re-emergence or recurrence of laryngomalacia at an older age rather than a true late-onset condition (4).

Other authors such as Richter et al. considered late onset laryngomalacia as a different entity from congenital laryngomalacia being more commonly than reported at the time their paper was published (6). Moreover, in their series, these older children had no previous symptoms or diagnosis of laryngomalacia.

3.3 Diagnosis of sleep-dependent laryngomalacia

Sleep-dependent laryngomalacia is typically diagnosed during drug-induced sleep endoscopy (DISE) and is commonly caused by inspiratory collapse of redundant supra-arytenoidal mucosa (type 1 laryngomalacia).

Drug-induced sleep endoscopy allows for a dynamic evaluation of the upper airway during drug-induced sleep and aims to reveal the site(s) of upper airway obstruction in children with OSA. Suspicion of sleep-dependent laryngomalacia is a well-established indication for DISE (26).

The case presentation above is in accordance with a disease continuum since

Figure 1: *Type 1 Laryngomalacia: inspiratory collapse of mucosa overlying the arytenoid cartilages. This is the most common type found in about 60% of infants and is typical for sleep-dependent laryngomalacia. A combination of types (ex type 1 and 2) may be present in the same infant.*

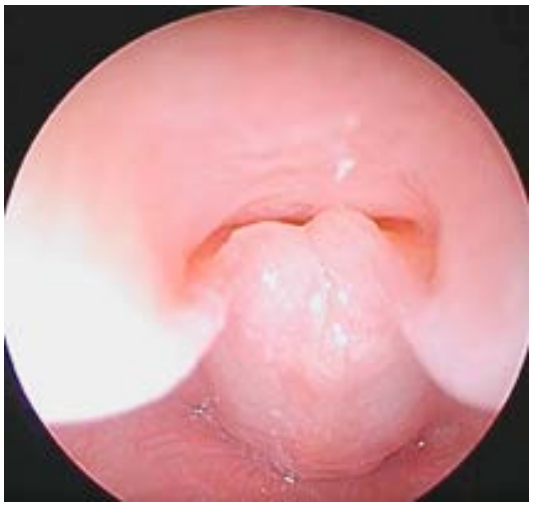


Figure 2: *Type 2: latero-lateral collapse of the epiglottis with short-aryepiglottic folds, present in about 20% of infants*

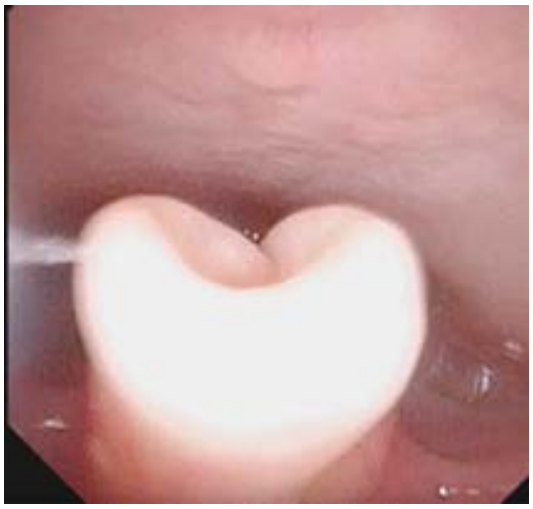
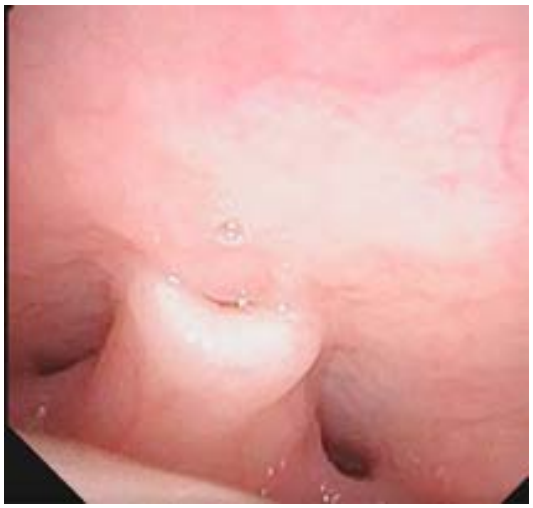


Figure 3: *Type 3: collapse of the epiglottis against the posterior wall, present in another 20% of infants.*



upon careful history taking, symptoms were noticed shortly after birth. This case also points toward the role of polysomnography in young children with unexplained obstructive breathing during the night and the importance of endoscopic examination under general anesthesia in those cases were PGS is abnormal but not explained by clinical features.

3.4 Sleep-dependent laryngomalacia and obstructive sleep apnea

The prevalence of laryngomalacia among children presenting with sleep-disordered breathing identified by sleep nasopharyngoscopy is 3.9% (25). Sleep-dependent laryngomalacia has been recognized as the second most common cause of persistent OSA following adenotonsillectomy (27).

In their first paper on sleep-dependent laryngomalacia, Richter et al. presented seven patients, mean age of 6.3 years in whom a diagnosis of sleep-dependent laryngomalacia was established by flexible and rigid bronchoscopy during spontaneous breathing under general anesthesia (6). They all presented with symptoms consistent with OSA and five of them had a history of prior adenotonsillectomy. Polysomnography confirmed a diagnosis of OSA with a mean apnea/hypopnea index of 6/hr.

A few years later, Revell and Clarke reported on sleep-dependent laryngomalacia as a cause of OSA (4). The authors describe 19 children with OSA in whom a diagnosis of laryngomalacia was established by airway endoscopy. These children presented with snoring, apneas, daytime somnolence and difficulties awakening as the most common symptoms. Over 2/3 patients had adenotonsillar hypertrophy on clinical examination and the youngest was three years and nine months old (beyond the age range of congenital laryngomalacia).

Digoy et al. investigated the contribution of laryngomalacia to OSA in children over 12 months of age (28). The authors reported on 43 children with OSA on polysomnography and sleep-dependent laryngomalacia confirmed by sleep endoscopy. The majority, 32 patients, had a history of prior adenotonsillectomy. Nine patients had an underlying syndrome and five had cerebral palsy.

Laryngomalacia is increasingly reported as a cause of treatment failure after adenotonsillectomy. Chan et al. analyzed the data of 24 children, mean age

7. 3 ± 0. 8 years with persistent OSA who underwent supraglottoplasty, 50% of them had a comorbidity and 29.2% were obese (2). A greater postoperative improvement in AHI was observed in children without comorbidities (16.1 /h versus 2.6/h) compared to those with comorbidities (13.8/h versus 7.3/h) after supraglottoplasty. The authors suggested that the presence of comorbidities is a risk factor for poor outcome after supraglottoplasty (2). The children in this study all presented with sleep dependent laryngomalacia identified through sleep endoscopy and were overall younger than those presenting with lingual tonsillar hypertrophy as a cause of persistent OSA. The younger age of these patients and the high percentage of children with medical comorbidities characterized generalized hypotonia, lead the authors to suggest that a deficiency in supraglottic tone is the cause of laryngomalacia.

3.4 Treatment of sleep-dependent laryngomalacia

When sleep-dependent laryngomalacia co-exists with a fixed upper airway obstruction such as adenotonsillar hypertrophy the clinician is facing a dilemma with respect to treatment. In some cases, the dynamic collapse of supraglottic tissues (laryngomalacia) is a secondary phenomenon caused by increased inspiratory negative pressure required to overcome the obstruction caused by adenotonsillar hypertrophy. In such cases with primarily adenotonsillar hypertrophy and mild laryngomalacia, the latter may resolve after adenotonsillectomy and supraglottoplasty may not always be necessary (4).

On the other hand, in meta-analysis by Camacho et al, 77.4% of children with laryngomalacia identified through DISE, had persistent OSA following adenotonsillectomy.(3)

Love and colleagues investigated the outcome of OSA treatment in surgically naïve young (< 2 year old) children with and without DISE identified laryngomalacia (29). The authors included 41 children with OSA and laryngomalacia (LM+) and 38 with OSA but no laryngomalacia (LM-). DISE directed treatment in the LM+ group consisted of supraglottoplasty in 92.3%, adenoidectomy in 46.2%, tonsillectomy in 26.3%. By contrast, in the LM- group DISE directed treatment consisted of adenoidectomy in 84.2%, tonsillectomy in 52.6% and 15.8% underwent no surgical intervention. Based upon post-operative PSG data, the authors concluded that DISE directed surgery reduced OSA severity in both groups.

Interestingly, children with OSA and laryngomalacia presented earlier in life and had worse quality of life by parental report.

Mase and colleagues investigated the impact of supraglottoplasty on OSA severity in patients with sleep-dependent laryngomalacia (5). Data were available for nine patients who underwent supraglottoplasty for sleep-dependent laryngomalacia and in whom pre-and post-treatment PSG data were available. The authors documented a significant improvement in AHI along with an improvement in weight to length percentiles and caregivers reported an improvement in sleep quality. A higher pre-operative AHI was associated with a greater postoperative improvement.

Both studies by Love et al. and Mase et al. underscore the role of sleep endoscopy to identify supraglottic obstruction, to avoid unnecessary adenotonsillar surgery and the role of supraglottoplasty as a treatment option for sleep-dependent laryngomalacia (5, 29).

Effect of supraglottoplasty on OSA in congenital and sleep-dependent laryngomalacia

Farhoud et al. performed a systematic review on the effect of supraglottoplasty for infants with congenital laryngomalacia and OSA (30). The authors included four studies, all level four evidence and could analyze data for 44 patients. Each study showed a statistically significant improvement in AHI. For patients with a pre- operative AHI greater than 12/h, the mean difference after supraglottoplasty was -30.7 and in those with a preoperative AHI less than 12/h, the mean difference after supraglottoplasty was -3.7. Both differences were statistically significant. In addition, there was a significant improvement in oxygen saturation nadir. The authors concluded that supraglottoplasty is a beneficial treatment option for infants with congenital laryngomalacia and OSA although patients may have persistent disease. A more marked improvement was observed in those with more severe disease at baseline and in younger patients (<7 months).

Camacho et al. performed a systematic review on the outcome of supraglottoplasty for laryngomalacia associated with OSA (3). The authors analyzed data from 138 patients, 74 with congenital and 64 with sleep-dependent laryngomalacia. About 77% of the children with sleep-dependent laryngomalacia had failed adenotonsillectomy.

In children with sleep-dependent laryngomalacia, AHI decreased from a mean of 14.0 ± 16.5 to 3.3 ± 4.0 events per hour and the lowest oxygen saturation improved from 84.8% ± 8.4 to 87.6 ± 4.4% after supraglottoplasty. In cases with congenital laryngomalacia, AHI decreased from 20.4 ± 23.9 to 4.0 ± 4.5 events/hour and the lowest oxygen saturation improved from 74.5 ± 11.9 % to 88.4 ± 6.6%. Based upon individual data available from 9 studies, it was derived that 10.5% of the patients with sleep-dependent laryngomalacia were cured after supraglottoplasty (AHI <1/h) whereas 26.5% of patients with congenital laryngomalacia were cured.

The outcome of supraglottoplasty on central apneas is reported in only a few papers. Verkest et al. presented data on pre-and post-treatment polysomnography in 17 patients (18). The central apnea index decreased from 1.8/h (0.7-3.5) at baseline to 1.3/h (0.3-2.5) after supraglottoplasty but this change was not significant. Similar findings were reported by Cortes et al. (20). These authors did not find a significant improvement in CAI one month after surgery in nine infants with severe laryngomalacia who underwent supraglottoplasty. Thanphaichitr et al. warned that some infants with laryngomalacia and CSA may require additional treatment beyond surgery such oxygen therapy or respiratory stimulants (16).

A summary of the main findings and areas for future research are listed in Table 1 and 2.

Conflict of interest

The author has no conflict of interest to declare.

Table 1: Main findings on laryngomalacia and sleep-disordered breathing

Congenital laryngomalacia	Sleep-dependent laryngomalacia
A high prevalence of sleep-disordered breathing has been documented by PSG	Identified as the cause of OSA in nearly 4% of children.
Polysomnography is a useful non-invasive tool to assess disease severity, guide therapeutic decision making and evaluate treatment outcome	Represents the second most common cause of persistent OSA after adenotonsillectomy.
Infants present with inspiratory stridor during wakefulness, apneas and increased work of breathing may be noticed during sleep.	Most cases are >2 years old, present with symptoms of OSA but do not have an inspiratory stridor during wakefulness Supraglottic collapse is only present during sleep.
A diagnosis of congenital laryngomalacia is established during awake flexible endoscopy and/or direct laryngoscopy under general anesthesia	Diagnosis established by drug induced sleep endoscopy.
Different types of laryngomalacia are described according to the pattern of supraglottic collapse	The typical feature is that of a type 1 laryngomalacia with inspiratory collapse of redundant supra-arythenoidal mucosa.
Supraglottoplasty improves polysomnographic parameters	Supraglottoplasty improves polysomnographic parameters but to a lesser extent than in congenital laryngomalacia

Table 2: Areas for future research

Congenital laryngomalacia	Sleep-dependent laryngomalacia
Is spontaneous resolution of inspiratory stridor associated with improvement of endoscopic findings and PSG parameters	What is the spontaneous evolution if left untreated?
What is the effect of supraglottoplasty on central apneas and what are treatment options if central apneas persist after surgery?	Is there a continuum in supraglottic collapse starting in infancy or is sleep-dependent laryngomalacia a different disease entity?

REFERENCES:

1. Isaac A, Zhang H, Soon SR, Campbell S, El-Hakim H. A systematic review of the evidence on spontaneous resolution of laryngomalacia and its symptoms. Int J Pediatr Otorhinolaryngol. 2016;83:78-83.
2. Chan DK, Truong MT, Koltai PJ. Supraglottoplasty for occult laryngomalacia to improve obstructive sleep apnea syndrome. Arch Otolaryngol Head Neck Surg. 2012;138(1):50-4.
3. Camacho M, Dunn B, Torre C, Sasaki J, Gonzales R, Liu SY, et al. Supraglottoplasty for laryngomalacia with obstructive sleep apnea: A systematic review and meta-analysis. Laryngoscope. 2016;126(5):1246-55.
4. Revell SM, Clark WD. Late-onset laryngomalacia: a cause of pediatric obstructive sleep apnea. Int J Pediatr Otorhinolaryngol. 2011;75(2):231-8.
5. Mase CA, Chen ML, Horn DL, Parikh SR. Supraglottoplasty for sleep endoscopy diagnosed sleep dependent laryngomalacia. Int J Pediatr Otorhinolaryngol. 2015;79(4):511-5.
6. Richter GT, Rutter MJ, deAlarcon A, Orvidas LJ, Thompson DM. Late-onset laryngomalacia: a variant of disease. Arch Otolaryngol Head Neck Surg. 2008;134(1):75-80.
7. Olney DR, Greinwald JH, Jr., Smith RJ, Bauman NM. Laryngomalacia and its treatment. Laryngoscope. 1999;109(11):1770-5.
8. Del Do M, Song SA, Nesbitt NB, Spaw MC, Chang ET, Liming BJ, et al. Supraglottoplasty surgery types 1-3: A practical classification system for laryngomalacia surgery. Int J Pediatr Otorhinolaryngol. 2018;111:69-74.
9. Sutherland GL, HL. Congenital laryngeal obstruction. Lancet. 1897;2.
10. Amin MR, Isaacson G. State-dependent laryngomalacia. Ann Otol Rhinol Laryngol. 1997;106(11):887-90.
11. Thompson DM. Abnormal sensorimotor integrative function of the larynx in congenital laryngomalacia: a new theory of etiology. Laryngoscope. 2007;117(6 Pt 2 Suppl 114):1-33.
12. Carter J, Rahbar R, Brigger M, Chan K, Cheng A, Daniel SJ, et al. International Pediatric ORL Group (IPOG) laryngomalacia consensus recommendations. Int J Pediatr Otorhinolaryngol. 2016;86:256-61.
13. Garritano FG, Carr MM. Characteristics of patients undergoing supraglottoplasty for laryngomalacia. Int J Pediatr Otorhinolaryngol. 2014;78(7):1095-100.
14. Richter GT, Thompson DM. The surgical management of laryngomalacia. Otolaryngol Clin North Am. 2008;41(5):837-64, vii.
15. Zwacka G, Scholle S, Kemper G, Rieger B. Nasal CPAP therapy for infants with congenital stridor. Sleep Breath. 1997;2(4):85-97.
16. Tanphaichitr A, Tanphaichitr P, Apiwattanasawee P, Brockbank J, Rutter MJ, Simakajornboon N. Prevalence and risk factors for central sleep apnea in infants with laryngomalacia. Otolaryngol Head Neck Surg. 2014;150(4):677-83.
17. Fard D, Rohlfing ML, Razak A, Cohen MB, Levi JR. Prevalence and natural history of obstructive sleep apnea in pediatric patients with laryngomalacia. Int J Pediatr Otorhinolaryngol. 2020;133:109967.
18. Verkest V, Verhulst S, Van Hoorenbeeck K, Vanderveken O, Saldien V, Boudewyns A. Prevalence of obstructive sleep apnea in children with laryngomalacia and value of polysomnography in treatment decisions. Int J Pediatr Otorhinolaryngol. 2020;137:110255.
19. Cortes MC, Villamor P, de la Torre Gonzalez C, Alvarez-Neri H. Complete polysomnographic parameters in infants with severe laryngomalacia prior to and after supraglottoplasty. Int J Pediatr Otorhinolaryngol. 2019;119:131-5.
20. Tawfik KO, Sedaghat AR, Ishman SL. Trends in Inpatient Pediatric Polysomnography for Laryngomalacia and Craniofacial Anomalies. Ann Otol Rhinol Laryngol. 2016;125(1):82-9.
21. O'Connor TE, Bumbak P, Vijayasekaran S. Objective assessment of supraglottoplasty outcomes using polysomnography. Int J Pediatr Otorhinolaryngol. 2009;73(9):1211-6.
22. Powitzky R, Stoner J, Fisher T, Digoy GP. Changes in sleep apnea after supraglottoplasty in infants with laryngomalacia. Int J Pediatr Otorhinolaryngol. 2011;75(10):1234-9.
23. Zafereo ME, Taylor RJ, Pereira KD. Supraglottoplasty for laryngomalacia with obstructive sleep apnea. Laryngoscope. 2008;118(10):1873-7.
24. Thompson DM. Laryngomalacia: factors that influence disease severity and outcomes of management. Curr Opin Otolaryngol Head Neck Surg. 2010;18(6):564-70.
25. Thevasagayam M, Rodger K, Cave D, Witmans M, El-Hakim H. Prevalence of laryngomalacia in children presenting with sleep-disordered breathing. Laryngoscope. 2010;120(8):1662-6.
26. Wilcox LJ, Bergeron M, Reghunathan S, Ishman SL. An updated review of pediatric drug-induced sleep endoscopy. Laryngoscope Investig Otolaryngol. 2017;2(6):423-31.
27. Manickam PV, Shott SR, Boss EF, Cohen AP, Meinzen-Derr JK, Amin RS, et al. Systematic review of site of obstruction identification and non-CPAP treatment options for children with persistent pediatric obstructive sleep apnea. Laryngoscope. 2016;126(2):491-500.
28. Digoy GP, Shukry M, Stoner JA. Sleep apnea in children with laryngomalacia: diagnosis via sedated endoscopy and objective outcomes after supraglottoplasty. Otolaryngol Head Neck Surg. 2012;147(3):544-50.
29. Love H, Slaven JE, Mitchell RM, Bandyopadhyay A. Outcomes of OSA in surgically naive young children with and without DISE identified laryngomalacia. Int J Pediatr Otorhinolaryngol. 2020;138:110351.
30. Farhood Z, Ong AA, Nguyen SA, Gillespie MB, Discolo CM, White DR. Objective Outcomes of Supraglottoplasty for Children With Laryngomalacia and Obstructive Sleep Apnea: A Meta-analysis. JAMA Otolaryngol Head Neck Surg. 2016;142(7):665-71.