Congenital Laryngomalacia: Disease Spectrum and Management

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Etiology

The precise etiology of the decreased laryngeal tone resulting in prolapse of the supraglottic tissues into the airway causing obstruction seen in laryngomalacia is unknown and continues to be an area of research. Theories of etiology include anatomic, cartilaginous, and neurologic origins. The anatomic theory suggests that the native laryngeal tissues are abnormal. The classic findings of shortened aryepiglottic folds, an omega-shaped or retroflexed epiglottis, and redundant arytenoid tissues seen in laryngomalacia (Figs. 1 and 2) may also present in infants without symptoms of laryngomalacia. Moreover, not all patients with laryngomalacia have these "abnormal" findings, challenging the validity of this theory.

The cartilaginous theory proposes that the cartilages of the infantile larynx are immature and have increased pliability. This theory has been refuted by histopathologic studies showing normal cartilage microanatomy in infants with severe laryngomalacia [1].

Published studies best support the neurologic theory of laryngomalacia which theorizes that neurosensorimotor dysfunction leads to decreased neuromuscular tone and coordination of the laryngeal structures leading to loss of laryngeal tone. An inference of a neurologic cause can be deduced from other conditions that affect the central nervous system leading to laryngomalacia or laryngomalacia-like clinical findings and symptoms. For example, central nervous system sedation can cause supraglottic obstruction in infants without laryngomalacia [2]. Moreover, late onset or acquired laryngomalacia has been seen to occur in children and adults who suffer a central nervous system insult such as a stroke, hypoxic brain injury, seizure, or trauma. Compression of the brainstem, like that of a Chiari malformation, has resulted in laryngomalacia with disease resolution following neurosurgical decompression [3]. It also is interesting to note that up to 20 % of infants with laryngomalacia have an associated neurologic abnormality [1, 3, 4].

Pathogenesis

Laryngeal tone and function is coordinated and modulated by a vagal nerve pathway called the laryngeal adductor reflex (LAR). Sensory information is gathered by superior laryngeal nerve fibers located in the aryepiglottic fold. Afferent signals pass through the nodose ganglion and are transmitted to the brainstem to synapses in the nucleus solitarius and nucleus ambiguous. These nuclei regulate breathing and swallowing. The efferent pathway is activated with signals propagating via the vagus nerve to the laryngeal muscles. In normal conditions, an involuntary motor response results in glottic closure and inhibition of respiration and swallowing, protecting the airway from the perceived laryngeal stimulus. This reflex also modulates baseline laryngeal tone. Abnormal sensorimotor integration of the LAR anywhere along the pathway results in decreased laryngeal tone, choking, aspiration, apnea, swallowing difficulty, and inability to clear secretions [1], all of which are within the spectrum of symptoms and clinical examination findings that may be seen in infants with laryngomalacia.

Laryngopharyngeal sensory testing in infants with laryngomalacia has demonstrated that the sensory stimulus threshold needed to begin the laryngeal adductor reflex is elevated in those with moderate and severe laryngomalacia. This finding suggests that peripheral afferent function and/or brainstem function are altered and lead to decreased laryngeal

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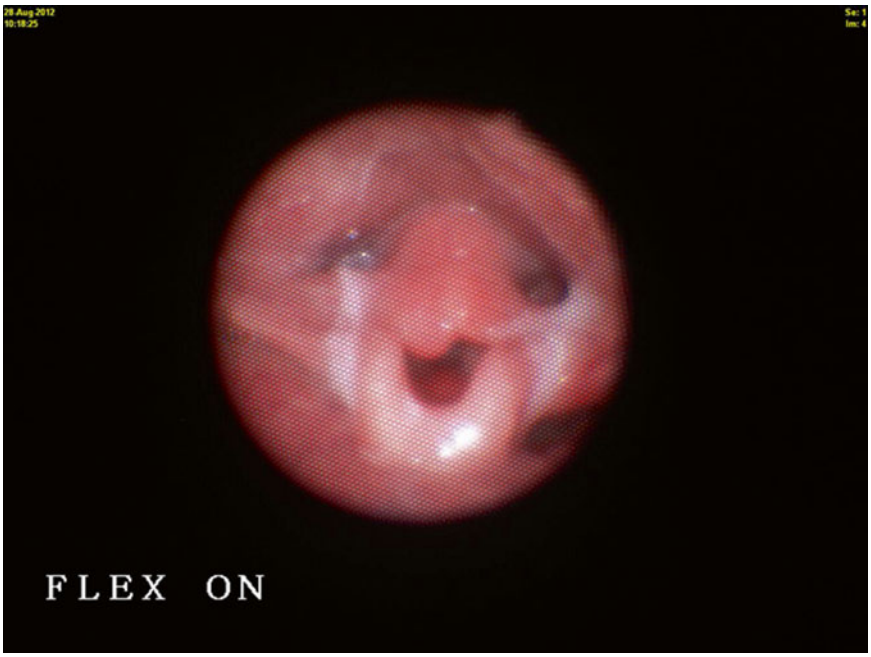

Fig. 1 Fiberoptic flexibible laryngoscopy with endoscopic evaluation of swallowing in a 2-month infant with laryngomalacia. Typical anatomic features including shortened aryepiglottic folds, bilateral supraarytenoid prolapse, posterior glottic edema, and posterior pharyngeal wall cobblestoning effect. Laryngeal penetration of formula seen over the aryepiglottic fold

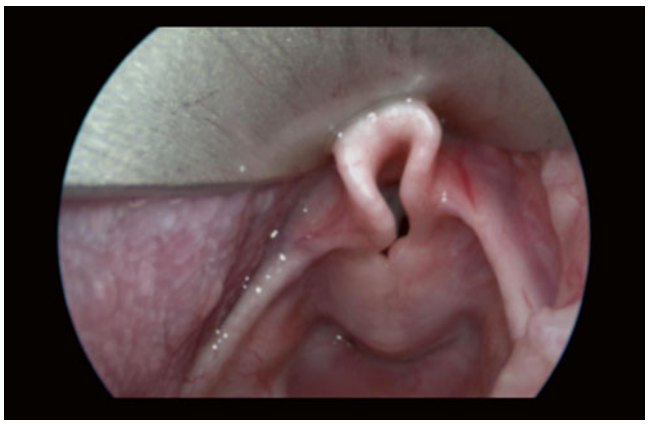

Fig. 2 Two-month child with severe laryngomalacia requiring supraglottoplasty. Typical features including omega-shaped epiglottis, short aryepiglottic folds, and arytenoid prolapse are seen

tone in patients with laryngomalacia. This theory is further supported by the finding of submucosal nerve hypertrophy in histological specimens of the supraarytenoid tissue in infants with severe laryngomalacia. It is unclear, however, if the noted nerve hypertrophy is the primary pathology or if it occurs secondary to inflammation from gastroesophageal reflux disease [4].

Alteration of brainstem responses may also contribute to the pathogenesis of laryngomalacia as they are often altered by states of hypoxia and hypercarbia, both of which may be seen in affected infants. The effect of brainstem modulation is further supported by case reports demonstrating reversal of laryngomalacia symptoms and findings after surgical decompression of the brainstem due to Chiari malformation or correction of a vertebral anomaly causing compression of the brainstem [3].

Gastroesophageal reflux likely plays an important role in the dysfunction of this neurological pathway by altering laryngeal sensation and causing tissue edema. Chronic acid exposure on the chemo- and mechanoreceptors of the larynx results in a functional denervation of the afferent response of the LAR. With decreased sensation the infant has difficulty handling secretions and initiating a swallow. Acid exposure also causes tissue edema, which can further exacerbate inspiratory prolapse of the supraglottic structures into the airway. Obstruction during inspiration can in turn increase negative intrathoracic pressure promoting further reflux and creating a vicious cycle. Until the airway obstruction/ reflux cycle is broken, the infant will continue to have symptoms.

Epidemiology

Laryngomalacia is the most common congenital laryngeal anomaly, and is implicated in 45–75 % of infants with stridor. The exact demographic data of laryngomalacia is not known. There is a reported male predominance of an average 1.6:1 male to female ratio [1, 5–10]. The clinical significance of this is unknown. No racial differences have been reported, but the majority of published literature has reported on Caucasian infants [11].

Congenital laryngomalacia can occur in newborns of any gestational age. The condition is seen in premature infants but has not been shown to have an increased incidence in this population. There may be a trend toward an association of

prematurity and severity of disease, but larger populations with documented gestational age data are lacking [1, 12]. When comparing the specific sites of supraglottic collapse, preterm infants were found to have more of the classic features of laryngomalacia compared to term infants [13].

Clinical Presentation

Laryngomalacia is characterized by inspiratory stridor secondary to supraglottic tissue prolapse. The disease typically presents with stridor within 2 weeks of birth. The symptoms gradually increase until a peak is reached at 6–8 months of age. The majority of cases are self-limited and resolve by 18–24 months of age, but up to 20 % of infants will have significant airway obstruction and/or feeding issues requiring medical and surgical treatment [1, 14, 15].

Stridor is the primary symptom of laryngomalacia. On inspiration a high pitched, fluttering stridor is heard as the supraglottic tissues collapse over the glottis and vibrate against each other. Laryngomalacia increases with crying, agitation, and feeding due to the increase of negative intrathoracic airway pressures during these times. Supine positioning increases symptoms secondary to the posterior displacement of the base of tongue and laryngeal structures.

Feeding difficulties including regurgitation, emesis, cough, choking, and slow feeding are the most common associated symptoms of the disease. Airway obstruction interferes with the infant's ability to coordinate the suck-swallow-breathe sequence needed for feeding. Weight loss and failure to thrive can occur when there is a high metabolic demand of feeding and breathing against an obstruction.

In severe disease, infants may also present with suprasternal and subcostal retractions, tachypnea, apneic pauses, cyanosis, pectrus excavatum, pulmonary hypertension, and cor pulmonale.

Disease Spectrum

Laryngomalacia is a spectrum categorized into mild, moderate, and severe forms. Upon presentation to a health care provider, 40 % of infants have mild, 40 % moderate, and 20 % have severe disease [15].

Infants with mild disease have stridor without respiratory compromise and occasional cough, choking, and regurgitation with feeding. Despite this, these infants have normal coordination of the suck-swallow-breathe sequence and have an average resting oxygen saturation of 98–100 % [15]. The majority (70 %) of infants with mild disease have an uncomplicated course and resolution but 30 % will have worsening of feeding associated symptoms and progression to moderate laryngomalacia [15].

Forty percent of infants present with moderate laryngomalacia, which is characterized by stridor and frequent feeding-associated symptoms. Coughing, choking, regurgitation, fussiness, and cyanosis frequently occur during feeds (Fig. 1). Aspiration and weight loss may ensue if feeding modifications and acid reflux therapies are not initiated. Infants with moderate laryngomalacia are not hypoxic, but they may have a lower resting SAO_2 (96 %) [1, 15]. Even with feeding modifications and acid suppression, 28 % develop severe disease [15].

Those with severe disease have stridor along with associated symptoms of recurrent cyanosis, apneic pauses, suprasternal and subcostal retractions, aspiration, and failure to thrive. These infants also have a lower resting SAO_2 of 88–92 %. If not appropriately managed these infants may develop pectus excavatum, pulmonary hypertension and/or cor pulmonale. Up to 30 % of infants will have severe laryngomalacia with an additional medical comorbidity such as neurologic disease, congenital heart disease. or a genetic or syndromic condition.

Diagnosis

Diagnosis of laryngomalacia is primarily made by history and confirmed by an awake flexible nasopharyngoscopy. Caregivers often give a classic history of high pitched inspiratory stridor beginning within weeks of birth. The stridor is exacerbated with crying, agitation, supine positioning, and feeding. It is important to ask about feeding symptoms including cough, choking, regurgitation, and slow/fussy feeds. History of suprasternal and/or subcostal retractions, cyanosis, apnea, aspiration, and failure to thrive are worrisome and indicate severe disease. Cardiac, pulmonary, neurologic, gastrointestinal disease and the presence of a genetic disorder or syndrome history are important to note for treatment planning and prognostication.

The infant's birth, intubation, and surgical history are important in determining congenital versus acquired causes of stridor. The differential diagnosis of congenital stridor in an infant includes subglottic stenosis, vocal cord paralysis, tracheomalacia, and tracheal stenosis. Conditions that cause inspiratory stridor in infants and can mimic laryngomalacia include unilateral vocal fold paralysis, vallecular cyst, or a saccular cyst of the larynx. These entities can be differentiated by flexible laryngoscopy. In contrast to the inspiratory stridor of laryngomalacia, infants with bilateral vocal fold paralysis or subglottic stenosis have biphasic stridor with both inspiratory and expiratory components. The stridor of tracheomalacia and tracheal stenosis has a characteristic expiratory phase.

As noted above, confirmation of laryngomalacia is made by an awake flexible nasopharyngoscopy (Fig. 1). The infant

is gently retrained on the caregivers lap in an upright or semi-reclined position. Sedation is not necessary, and may lead to false positive findings due to the resultant decrease in neuromuscular tone. A flexible scope is passed and the nasopharyngeal, oropharyngeal, hypopharyngeal, and laryngeal structures are inspected.

During the procedure, arytenoid mucosa and cartilage prolapse, shortened aryepiglottic folds and an omega or tubular epiglottis may be visualized. A retroflexed epiglottis with posterior pharyngeal contact can also be seen in more severe cases. One must visualize dynamic collapse of the supraglottic structures on inspiration and obtain a consistent history to diagnosis laryngomalacia. The presence of an omega-shaped epiglottis is not pathognomonic for laryngomalacia as up to 50 % of normal infants have this shape to the epiglottis [16]. Inspiratory stridor is heard during a positive exam. In severe disease the infant may also exhibit retractions and/or brief cyanosis.

The larynx may prolapse at one or multiple supraglottic locations. Multiple anatomic classification systems have been described based on the supraglottic location and direction of collapse [13, 17–19]. When redundant arytenoid mucosa and accessory cartilages prolapse, this is recognized as posterior prolapse. Foreshortened aryepiglottic folds obstruct the airway in the lateral plane, and anterior collapse occurs with posterior displace of the epiglottis. The pattern of collapse may help to guide surgical treatment.

After confirmation of the diagnosis, other adjuvant studies may be indicated depending on symptomatology and severity of disease. Videofluoroscopic swallow study or functional endoscopic evaluation of swallow (FEES) can be used to assess feeding symptoms and aspiration. In infants with known chronic aspiration, a chest X-ray should be obtained to determine the amount of pulmonary injury present. Concomitant gastroesophageal disease such as malrotation or pyloric stenosis should be ruled out with an esophagram in those with severe recurrent emesis.

Secondary Airway Lesions

Infants with laryngomalacia have a 7.5–64 % chance of having a secondary or synchronous airway lesion [20–24]. The wide range of incidence is likely due to the technique used to identify a secondary lesion and indication for screening. The most frequently identified lesions are tracheomalacia, subglottic stenosis, and vocal cord paralysis. The incidence of secondary lesions increases in congenital syndromic disorders such a Down syndrome.

Secondary lesions are associated with increased laryngomalacia severity and progression of disease which leads to a higher likelihood of requiring a surgical intervention. Secondary lesions add an additional level of obstruction thereby changing airflow dynamics. Increased resistance in the distal airway can exacerbate the degree of obstruction to the glottic level by means of the Venturi principle.

Secondary anomalies can also potentiate gastroesophageal reflux disease [14, 15, 21, 22]. Infants with mild to moderate disease that have a secondary lesion are 4.8 times more likely to need a surgical intervention [21]. Eliminating supraglottic obstruction with a supraglottoplasty allows the airflow at the secondary lesion to be more favorable. By performing a supraglottoplasty, the clinical significance of secondary lesions may decrease and eliminate the need for surgical treatment.

As lesions distal to the vocal folds are difficult to accurately diagnosis by flexible laryngoscopy alone, further studies may be indicated in certain infants. High-kilovoltage airway radiographs can be used in screening for a fixed obstruction such as subglottic stenosis; whereas, airway fluoroscopy are appropriate if there is a suspicion of dynamic tracheomalacia. Although awake flexible laryngoscopy with tracheoscopy in the office has been described in the literature, we do not routinely advocate this technique in infants [25]. The gold standard of secondary lesion diagnosis is rigid laryngoscopy and bronchoscopy. This evaluation can be used in conjunction to a planned supraglottoplasty or performed before a supraglottoplasty if the diagnosis is in question.

Management

Most infants with laryngomalacia have mild to moderate symptoms (80–90 %) and do not require surgical intervention [1, 14, 26]. Infants with mild disease can be expectantly managed by their pediatricians, and parents should be reassured.

Treatment should be initiated for those with frequent feeding symptoms. Feeding modifications and acid suppression therapy are the primary means of treatment. Strategies to improve feeding symptoms include pacing with frequent burping, texture modification by thickening formula/breast milk, and upright positioning for feeding. Bottle feeding is sometimes preferred over breast feeding because the amount of milk released is more controlled.

Acid suppression treatment often decreases the feeding symptoms and may shorten the natural course of the disease [1]. Gastroesophageal reflux treatment decreases supraglottic edema and the resultant increase in upper airway obstruction. The dose and duration of therapy has not been studied prospectively. Treatments regimens that have been proposed are proton pump inhibitor therapy, H2 receptor antagonist therapy, and combination of the two. An average of 9 months of acid suppression therapy is typically given. The response to medical therapy can be

assessed by history and repeat physical exam. Up to 72 % of infants with moderate disease will have resolution of their symptoms within 12 months of using these management strategies [1, 15].

Those with severe laryngomalacia or worsening of moderate disease warrant surgical intervention [1, 14]. Surgical management is indicated in those who present with recurrent cyanosis, apneic pauses, severe suprasternal and subcostal retractions, aspiration, failure to thrive, pectus excavatum, pulmonary hypertension, and/or cor pulmonale. Infants who have worsening of their disease severity over time despite feeding modifications and acid suppression therapy are also candidates for surgical management. The primary operation use to manage laryngomalacia is a supraglottoplasty. Tracheostomy can be performed to definitively bypass the obstruction, but is reserved for those that have failed supraglottoplasty or have multiple other medical comorbidities that necessitate tracheostomy placement.

Multiple tools can be used to perform a supraglottoplasty, but the basic surgical principles remain the same regardless of instruments used. Briefly, the child is placed under mask ventilation with inhalational anesthetics. The otolaryngology and anesthesia team should be prepared for worsening obstruction during sedation. The airway should be fully evaluated for a secondary airway lesion with rigid laryngoscopy and bronchoscopy. The larynx is then visualized using a laryngoscope and laryngeal suspension system. The Benjamin-Lindholm or Parson's laryngoscopes are preferred by the authors as they give a wide view of the supraglottic structures. Insufflation of anesthetic gases and oxygen can be given via the side port of most laryngoscopes. The operative microscope is then brought into the field to allow for bimanual instrumentation and magnification during the procedure.

The aryepiglottic fold is incised at the base of the epiglottic cartilage. Prolapsed supraarytenoid mucosa is then removed bilaterally with a wedge resection. A cuff of mucosa should be maintained between the aryepiglottic fold incision and the arytenoid resection. Corniculate and cuneiform cartilages can also be removed with the wedge of supraarytenoid mucosa. Care must be taken to preserve the intra-arytenoid tissue and not violate the pharyngoepiglottic fold. In cases of shortened aryepiglottic folds and redundant arytenoid tissue, these procedures should result in a widened supraglottic airway.

These surgical maneuvers can be performed with cold steel microlaryngeal instruments or CO_2 laser depending on surgeon preference. Statically there is no difference between the outcomes of cold steel or CO_2 laser. CO_2 laser may give the surgeon better precision and hemostasis, but hemostasis does not tend to be significant risk during cold steel supraglottoplasty [14, 27, 28]. The risk of using the CO_2 laser includes airway fire, thermal injury, and theoretical risk of damage to the neural receptors of the supraglottic tissues which may lead to decreased laryngeal sensation.

Postoperative airway control depends on the age of the child, severity of disease, and extent of surgery performed. The patient may be extubated on the operating room table or remain intubated for a period of observation with planned extubation the following day. In infants younger than 1 year of age, overnight intubation with administration of a steroid dose before extubation is the recommended preference of the authors. Other experienced pediatric otolaryngologists extubate at the time of the procedure when safe, regardless of age. Racemic epinephrine may also be required at extubation.

When patients are tolerating room air and eating appropriately, they can be discharged to home. The authors recommend follow-up in appropriately 2 weeks. At that time, an assessment of weight gain and airway symptoms is important. A flexible laryngoscopy may be considered to assess surgical results and to assure the site is healing without granulation tissue. Postoperatively patients are continued on acid suppression medications for a minimum of 1 month. As symptoms and edema improve the reflux medications can be weaned. Functional endoscopic swallow evaluation and videofluoroscopy swallow studies are indicated for continued feeding difficulties or aspiration following surgery.

Complications following supraglottoplasty are rare; an 8 % complication rate is quoted in the literature [29]. Possible surgical site issues involve the development of granulation tissue, abnormal mucosal healing with webbing, bleeding, and infection. Supraglottic stenosis is a possible complication of supraglottoplasty which is difficult to manage. It reportedly occurs in 4 % of patients and is thought to be related to violation of the intra-arytenoid area or pharyngeoepiglottic fold [29]. Systemic events that may complicate the procedure include aspiration, bronchiectasis, bronchiolitis, and pneumonia.

The success rate of supraglottoplasty is as high, and up to 94 % of infants have resolution of their symptoms [14]. Revision may be required in 19–45 % of infants. Infants with neurologic disease, cardiac disease, congenital syndromes, and secondary airway lesion are more likely to need revision supraglottoplasty and possible tracheostomy. These specific considerations are discussed later in this chapter [1].

Multidisciplinary Considerations

Gastrointestinal Disease

Gastroesophageal reflux is noted in 65–100 % of infants who have laryngomalacia [1, 12, 15]. Infants with moderate and severe disease should be started on empiric reflux therapy with a proton pump inhibitor, H2 receptor antagonist, or a

combination of the two therapies. Feeding modifications to reduce reflux such as upright positioning and frequent burping are recommended. When these measures are not effective, gastroenterology consultation should be sought. In severe cases, pediatric surgery may consider fundoplication for those with continued refractory symptoms despite supraglottoplasty and maximum dose of acid suppression therapy [14].

Neurologic Disease

Neurologic disease is present in 20–45 % infants with laryngomalacia and when present may benefit from neurologic consultation [15]. Common neurologic comorbidities include hypotonia, developmental delay, cerebral palsy, mental retardation, microcephaly, and Chiari malformation. The association of neurologic disorders and laryngomalacia is not fully understood but is likely due to decrease of vagal-mediated laryngeal tone at the level of the brainstem. Infants with neurologic disease have increased severity of disease and a higher rate of surgical intervention. Revision supraglottoplasty is required in up to 70 % and tracheostomy in 60 % of those with neurologic comorbidities [30]. Those with persistent aspiration and severe symptoms after supraglottplasty should undergo MRI of the head to evaluate for brainstem or other CNS disease contributing to etiology.

Cardiac Disease

Congenital cardiac disease can be seen in up to 10 % of those with laryngomalacia and may exacerbate cyanosis, apnea, and respiratory distress when present [1, 15, 31]. Coordination of care with the patient's cardiologist and cardiac anesthesiologist may be necessary. Up to 34 % of infants with coexisting severe laryngomalacia and cardiac disease may require surgical treatment [1, 32]. Supraglottoplasty failure and subsequent tracheostomy is higher in this group of patients.

Congenital Anomalies/Syndromes/Genetic Disorders

Congenital anomalies and genetic disorders occur in 8–20 % of those with laryngomalacia [17, 31]. Down syndrome is the most commonly reportedly genetic disorder associated with the disease with 50 % of Down syndrome infants with respiratory symptoms having laryngomalacia [33, 34]. CHARGE association (coloboma, heart defect, chonal atresia, retardation, genital and ear abnormalities) and Pierre Robin sequence have also been associated with laryngomalacia. These syndromes are manifest with micrognathia which worsens laryngomalacia due to tongue base collapse into the hypopharynx. A supraglottoplasty in the setting of micrognathia is usually unsuccessful. Tracheostomy may be needed in these infants until their mandible grows or an advancement procedure is performed. Variants of 22q11.2 microdeletion syndrome are known to have upper airway obstruction which can be managed with a supraglottoplasty [3, 34, 35]. Cervical vertebral anomalies are common in this patient population and compression of the brainstem should be investigated as a possible cause of laryngomalacia.

Future Directions

Although laryngomalacia is a common anomaly, the exact neurologic etiology is still unknown. Research continues to focus on the role of the central nervous system, the peripheral nervous system, and the coordination of the two systems. The relationship between gastroesophageal reflux disease and laryngomalacia has been well proven, but standardized medical therapy and length of treatment has yet to be studied prospectively. Ongoing research to classify and describe the nature and anatomic pattern of collapse may better categorize patients by severity of disease. In the future, supraglottoplasty may be tailored to the type of collapse.

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