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Unilateral Vocal Fold Paralysis in Children: State-of-the-Art Treatment

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Abstract
Purpose of the Review The goal of this chapter is to present the most up-to-date options in managing unilateral vocal fold paralysis (VFP) in the pediatric population. As this condition affects multiple systems, and options are multiple, it is important to be aware of the potential risks and benefits of each possibility in order to facilitate informed decision making.
Recent Findings The use of laryngeal electromyography in the workup of VFP has more recently been popularized as an adjunct in the diagnosis and prognosis for recovery. Moreover, advances in laryngeal reinnervation surgery show promise in the pediatric population. Finally, laryngeal pacing and the use of fibroblast growth factors are important new future directions in the field.
Summary Management of unilateral vocal fold paralysis in children can be challenging with many treatment options available. A personalized and tailored approach to each patient is warranted.

Keywords Vocal fold paralysis · Dysphonia · Laryngology · Voice · Pediatric · Medialization · Laryngoplasty

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Introduction

Unilateral vocal fold paralysis in children has multiple implications from a clinical standpoint. Restoring functional swallowing, breathing, and voicing in this population can be challenging. Multiple therapeutic options are available, and this chapter focuses on presenting the most up-to-date, state-of-the-art treatment. A tailored approach, based on the characteristics of each presentation, should be favored.

Epidemiology

It is estimated that a pediatric otolaryngologist will encounter 4–10 cases per year of vocal fold paralysis (VFP) during the course of their practices [1]. This condition has important implications in terms of morbidity [2]. Speech, swallow, and respiratory functions can be affected.

The incidence of unilateral VFP has increased over the last decade, perhaps attributable to increased awareness and recognition of symptoms. The increased rate of premature infant survival ([3, 4] as well as better availability of flexible laryngoscopy have also been mentioned as factors for earlier diagnosis [5]. The advances in managing neurological and cardiac conditions in neonates contribute to this increased rate of diagnosis and incidence [2]. For example, the incidence of recurrent laryngeal nerve injury has been reported to be around 1.1% in a recent review [6].

Etiology

The first step in managing this condition is proper diagnosis and establishing a clear distinction between vocal fold (VF) immobility and VF paralysis. It is important to clarify the difference

between cricoarytenoid (CA) joint fixation and VF paresis and immobility. Suspension laryngoscopy and palpation can also help with the diagnosis as this helps to rule out mechanical fixation. Laryngeal electromyography (EMG), discussed later in this chapter, can also be a helpful diagnostic tool.

Once paralysis is established, the causes can be broadly divided into congenital or acquired etiologies. VFP represents 10% of congenital anomalies of the larynx [3–5, 7].

Iatrogenic injuries such as cardiothoracic procedures (for example PDA ligations, TEF repairs) or other neck surgeries can also result in VFP [4, 8, 9]. Birth trauma also accounts for a possible iatrogenic cause of VFP, when forceps are used in the setting of deliveries [7]. In a recent series published by Jabbour et al., cardiac surgeries were responsible for 68.8% of the cases (unilateral and bilateral VFP combined), while 21% of the cases were deemed of idiopathic origin. 7.4% of the cases were of neurologic etiology [2].

Malignancies of the surrounding anatomical structures (esophageal, thyroid, or lung), as well as infections (e.g., Lyme disease, Varicella zoster virus infection), represent other much less common causes. Finally, chemotherapy (vincristine toxicity is a commonly implicated agent) and birth related trauma are other etiological factors to be considered in a pediatric population.

Central nervous system abnormalities, such as Arnold Chiari malformations, can also result in the very early manifestation of vocal fold paralysis, in the setting of bilateral VFP [4].

Clinical Implications and Consequences

The larynx is involved in three critical functions: swallowing, phonation, and respiration [9].

Swallowing function can be affected in up to 25 to 47% of children with VCP [2, 4]. Recurrent aspiration can potentially lead to recurrent pneumonias and multiple hospitalizations that have financial consequences as well as long-term effects on pulmonary function [10]. Dysphagia can also lead to a significant decrease in calorie counts and can be seen as a significant psychological stressor on patients and their parents, putting patients at risk for possible failure to thrive.

It has been reported in the literature that up to 25–47% of pediatric patients with unilateral VCP show signs of dysphagia. Finally, respiratory issues have been reported to occur in 54 to 75% of pediatric patients [2, 4].

Patients with unilateral VCP can have increased breathiness, hoarseness, and straining, as well as muscle tension [11]. Dysphonia affects 50 to 61% of children with unilateral VCP [2, 4]. Dysphonic children cannot effectively communicate with their peers and it can negatively impact his or her growth and development. It has been reported that some children have expressed suicidal ideations and emotional disturbance secondary to their vocal problem [12]. Therefore, it is clear that this symptomatology can be harmful to patients and their families not only on a personal level, but also has a significant cost burden when we consider their multiple doctor visits and/or hospital admissions.

Respiratory function is also affected in this pediatric population. Unilateral or Bilateral VFP is the second most common cause of neonatal stridor, after laryngomalacia [1]. It has also been cited as the most frequent initial presenting symptom [7]. Patients can also demonstrate cyanotic episodes, apnea, and retractions [4]. These latter manifestations are more commonly seen in patients who have bilateral VFP, cardiac, and neurologic comorbidities [7].

Management Options and Outcomes

Spontaneous Recovery and Laryngeal Electromyography (EMG)

The natural history of a unilateral paralyzed fold is compensation by the contralateral side in 80% of the cases, all etiologies confounded [1]. Moreover, the rate of spontaneous recovery of the ipsilateral fold varies in the literature from 28 to 73% [2, 13]. Spontaneous recovery happens more often in children than in adults [4]. Unfortunately, there remains a good proportion of patients in which this does not occur (20%). These patients have a persistent glottal opening which put them at risk for respiratory, swallowing, and communication challenges.

Laryngeal EMG is a diagnostic tool that has been well studied and implemented in the adult population, but has not been used widely in pediatric patients. In children, the procedure often requires general anesthesia due to difficulty tolerating percutaneous needle insertions in the office setting. Electrodes are placed in the thyroarytenoid (TA) and posterior cricoarytenoid (PCA) muscles [14].

Typically, it is recommended that laryngeal EMG be performed 3 to 6 months after an iatrogenic injury. This delay is the recommended consensus as nerve injury can be imperceptible initially on EMG. Moreover, denervation may become evident only after a period of time [14]. However, if the cause of the VFP is idiopathic or congenital, then it should be done in a serial manner to assess the function over time [15]. There is a wide range of spontaneous recovery reported, up to 11 years in the literature, making it challenging to determine the optimal timing of performing surgical interventions in these patients [14].

The shortcomings of this diagnostic tool are the need for an operating room setting and the uncertainty of exact needle placement. Moreover, the readings and recordings are done in a non-volitional fashion, making the results slightly less reliable, as the patient is not phonating when asked to do so.

Finally, intercostal muscle recordings also need to be done for more accurate data collection [16].

Conservative Management: Voice Therapy

Multiple treatment options are available to address unilateral VCP. Voice therapy with a speech language therapist is usually the first line of treatment, unless patients show aspiration. Voice therapy has even been shown to improve glottal gap closure in a pediatric population [4]. This option is often age-dependent taking into account willingness and capability of the patients in attending multiple therapy sessions [17].

Surgical Interventions

The main goal of surgical interventions currently performed is medialization of the paralyzed vocal fold. These procedures do not restore the vocal fold movement [4]. The most common procedures are injection laryngoplasty, thyroplasty, or reinnervation procedures.

Injection Laryngoplasty

Injection laryngoplasty is the simplest, least invasive of these three options, and can provide prompt results, although they are short term. A material is injected in the paraglottic space in order to close the glottal gap [18]. This technique may require multiple injections depending on the product used: there is a gradual relateralization process that occurs as well as possible formation of fibrosis or scar formation with time [15]. The timing depends on the product that is used. For example, calcium hydroxyapatite (Radiesse) resorbs within 18 months on average [18, 19]. Multiple other filler options are currently available: cadaveric dermis, hyaluronic acid, bovine collagen, gelatin powder, or autologous fat are some examples [12, 18]. The duration of the injection can vary from 4 weeks to 9 months, depending on the chosen material (Table 1). There is no current guideline on which product needs to be used, and pediatric laryngologists' preferences vary.

Injection laryngoplasty is advantageous in patients for whom recovery is expected [12]. Laryngeal electromyography (EMG) can be done preoperatively in order to determine the prognosis of recovery of a VCP [4]. Injection laryngoplasty can be an adjunct therapy in neonates who present with recurrent aspiration, as the recovery rate of VCP might be increased in this subgroup of the pediatric population. It is in the senior author's experience that these patients might show rapid resolution as the issue seems to sometimes be related with paresis more than frank paralysis [15].

Another advantage of injection laryngoplasty is that it can be repeated in patients who are very young until their growth allows for more advanced or invasive laryngeal framework surgery and that it can be performed under local anesthesia in the more compliant and older child [12].

Relative contraindications to the procedure include patients for which it is hard to obtain proper laryngeal exposure, such as in syndromic or dysmorphic children. Neonates who are not aspirating should also not be injected, as their potential for recovery is higher [15].

Medialization Thyroplasty

Medialization thyroplasty is within the category of laryngeal framework surgery: the result is static and fixed as the paralyzed fold is medialized towards its counterpart. This is different than injection laryngoplasty in multiple regards: It involves an external neck incision, and the implanted material does not resorb with time [1]. The anatomical landmarks used in the adult population usually have to be adjusted in children [4]. Implantation of the chosen material has to be made more inferior to the usual landmarks [12, 23]. In the pediatric population, it is generally considered for patients who still require medialization after multiple injections, or for older children who can tolerate it and who show signs of aspiration. Teenagers might tolerate the awake procedure but in the senior author's experience, many teenagers simply cannot fully comply and alternative procedures such as nerve reinnervation remain attractive.

Medialization thyroplasty is generally done under general anesthesia in the pediatric population. The use of a laryngeal mask airway (LMA), combined with a flexible laryngoscopy, allows visualization of the vocal folds with the patient asleep [12]. The challenge is to be able to obtain a vocal satisfactory result with no feedback from the patient. Moreover, this procedure in children is often performed for aspiration when nerve reinnervation is not an option. This situation could

Table 1 Most commonly used materials for injection medialization thyroplasty in children

Product	Material	Duration
Radiesse voice gel	Carboxymethycellulose	1–3 months [20]
Radiesse	Calcium hydroxyapatite	18 months [20]
Restylane	Hyaluronic acid	2–4 months [20]
Juvederm	Hyaluronic acid	4–6 months [21]
Prolaryn plus	Calcium hydroxyapatite	Up to 12 months [22]
Prolaryn gel	Aqueous, glycerin, and carboxymethylcellulose gel	3–6 months [22]

occur when, for example, a patient had multiple prior cervical surgeries and ansa is not available for grafting.

Different options of implant material are available including Goretex or Silastic. Disadvantages of medialization thyroplasty include potential implant migration or extrusion (varies from 0 to 9.8% [24]), foreign body reactions (mostly seen previously with Teflon granuloma, now not used anymore), and concern for disruption of laryngeal development [17].

Reinnervation Procedures [12]

The most exciting development for unilateral VFP with promising results in the last 5 years is laryngeal reinnervation. The most common procedure is anastomosis of the ansa cervicalis to the recurrent laryngeal nerve (ANSA-RLN). Outcome studies in adults and now children demonstrate increased muscular tone [5, 25] without restoration of motion in the vocal fold.

Advantages of reinnervation include avoidance of foreign material implants, improvement in tone with potential beneficial impacts on pitch and loudness, and avoidance of vertical mismatch that can be a risk of thyroplasty surgery.

A disadvantage of reinnervation is that it takes 3 months to 1 year to be able to assess the results of this procedure. This is why the senior author of this chapter recommends injection laryngoplasty at the same time as reinnervation procedure.

In 2012, a series of 13 pediatric patients demonstrated encouraging results: improvements in both GRBAS (Grade, Roughness, Breathiness, Asthenia, Strain) scores and in parental assessment [27]. In 2015, Farhood et al. reported good objective vocal outcomes in a series of three operated pediatric patients. Improvements in shimmer and noise to harmonic ratios were reported, as well as subjective vocal improvements [8].

In 2016, Smith and Houtz published a series of 35 pediatric patients: Again, GRBAS scores and patient questionnaires also showed a favorable outcome [18]. However, they did not find a correlation between age of reinnervation and the vocal outcome.

Zur et al. [17], in her series of 33 patients, demonstrated that reinnervation resulted in improved long-term (14 months posttreatment measures) acoustic and perceptual results when compared to laryngeal injection groups.

Future Directions and Next Steps in Research

The ideal treatment for unilateral VCP in the pediatric population has not yet declared itself. Such a treatment should be long lasting and have a positive outcome on the vocal quality of the child. It should also have a positive impact on swallowing function, and no detrimental influence on the respiratory function [26].

Fibroblast Growth Factor Injections

In theory, the best treatment would be one that does not require repeated visits to the operating room, especially considering the newest evidence on the potential neurotoxic effects and neurodevelopmental outcomes in young children after general anesthesia [28, 29].

In the last few years, promising advancements have been made in the area of regenerative medicine. Fibroblast growth factor (FGF) injections have been demonstrated to have a positive impact on the growth of the vocal folds in adults. Evidence shows that FGF stimulate the production of hyaluronic acid by the fibroblasts of the vocal folds, while suppressing the production of collagen [30]. FGF injections have already shown improvements in adults with hoarseness caused by UVFP [30–32]. The proposed theory in the literature is that FGF could be absorbed by muscle cells within the laryngeal framework and therefore stimulate their growth [31]. An increased muscle tone could improve swallowing function and airway protection. Investigation of this route in a pediatric population could certainly yield important progress in the field.

Laryngeal Pacing Procedures for Bilateral Vocal Fold Paralysis

This chapter has focused on the management of unilateral vocal fold paralysis. However, innovative and exciting developments in the treatment of bilateral vocal fold paralysis are worth mentioning. Laryngeal pacing (LP) is based on the stimulation of the abductor branches of the RLN: In 2017, Muller et al. published a series of nine subjects (prospective first-in-human study) unilaterally implanted. The phonatory function did not seem to be improved by the pacing. However, a significant improvement was measured in the patient's respiratory function. The peak expiratory flow of these patients was better with the pacing [14, 15, 33, 34••]. At the moment, there is no application of this for pediatric unilateral vocal fold paralysis.

Conclusion

In summary, the treatment of unilateral VCP in the pediatric population remains a challenge due to the balance of critical functions including breathing, swallowing, and communication/voice. Injection laryngoplasty, medialization thyroplasty, and reinnervation procedures are the most common surgical treatments currently being utilized. Reinnervation procedures have been gaining in popularity in the last 5 years and further investigation is needed to help clarify its role and indication in the affected child. Future directions include the study of growth factor injections in the paralyzed folds of the pediatric population.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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34.•• Mueller AH, et al. Laryngeal pacing for bilateral vocal fold paralysis: voice and respiratory aspects. Laryngoscope. 2017;127(8):1838–44. **Laryngeal pacing is one of the most recent and new developments in the field of vocal fold paralysis. This is a landmark article on the topic**