



A Review of Treatment of Bilateral Vocal Fold Movement Impairment

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Abstract

Purpose of Review Bilateral vocal fold immobility is a challenging life-threatening problem involving multiple treatment options and nuanced clinical decision making. We aim to provide relevant background on the etiology, diagnosis, and management of bilateral vocal fold movement impairment (BVFMI).

Recent Findings Over the last 20 years, the management of bilateral vocal fold immobility has advanced significantly with the addition of multiple endoscopic approaches as well as procedures with the goal of returning dynamic function to the larynx, among them: selective reinnervation. Chemodeneration has also demonstrated promising results as a temporizing procedure in appropriately selected patients with BVFMI.

Summary Tracheostomy remains the mainstay of emergent treatment for airway obstruction secondary to bilateral vocal fold immobility. However, recent advances in endoscopic approaches allow for avoidance of tracheostomy in many patients. Developments in dynamic procedures with the aim of restoring laryngeal function allow for adequate airway management while maintaining voice quality and limiting aspiration risk.

Keywords Bilateral vocal fold mobility impairment · Vocal fold paralysis · Laryngeal Reinnervation · Chemodeneration · Static airway surgery

Introduction

Vocal fold function is crucial for survival. Impairment can result in dysphagia, aspiration, and most notably airway obstruction particularly when both vocal folds are involved [1]. Awake laryngoscopy provides a key tool for the assessment of vocal fold function and mobility. Decreased mobility is often labeled as paralysis or paresis, but these labels specifically refer to a lower motor neuron dysfunction contributing to

absent or abnormal vocal fold mobility. In reality, vocal fold movement is much more complex, and motion impairment may occur due to dysfunctional innervation resulting in laryngeal synkinesis and not complete denervation [2]. As a result, a better term to describe vocal fold “paralysis” is “vocal fold movement impairment.”

Bilateral vocal fold movement impairment (BVFMI) can be life threatening especially if the onset is acute. Initial management frequently consists of intubation or a tracheostomy to

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secure the airway [3]. Sometimes the voice is normal or near normal, though significant dyspnea and even overt biphasic stridor can occur. The problem can begin suddenly, such as on extubation after thyroidectomy, or it can develop insidiously [4]. An overview of the problem of BVFMI will be given, with emphasis on the variety of treatment options for management of BVFMI from infant to adult.

Etiologies (Table 1)

The most common causes of BVFMI differ between adults and children. Adults often present with new onset vocal fold immobility most commonly secondary to surgical trauma. Previous reviews have demonstrated 25–58% of BVFMI cases occur following surgery. Thyroidectomy is the most common surgery to result in BVFMI with parathyroid surgery being the second most common surgical procedure. Malignancy is the second most common etiology of acquired BVFMI ranging from 7 to 17% of cases [1, 5–7]. Intubation is also a common factor contributing to BVFMI and is thought to contribute to 2–18% of cases. A central nervous system disease or tumor can also result in bilateral vocal fold paralysis. Other important factors to consider in adults should include non-surgical trauma, rheumatoid arthritis, other autoimmune diseases, radiation therapy, and infection. Finally, when a cause cannot be identified, idiopathic bilateral vocal fold immobility occurs in 3–13% of cases [1, 6–8].

Table 1 Etiology of bilateral vocal fold immobility

Congenital	Acquired
Central nervous system	Trauma
Arnold Chiari	Surgical trauma
Syringomyelia	Thyroidectomy
Syringobulbia	Parathyroidectomy
Leukodystrophy	Tracheoesophageal fistula repair
Encephalocele	Blunt trauma
Hydrocephalus	Infectious
Cerebral Dysgenesis	Post-poliomyelitis
	Tuberculosis
	Cytomegalovirus
	West Nile virus
Peripheral nervous system	Peripheral nervous system
Congenital myasthenia gravis	Guillain-Barré syndrome
	Myasthenia gravis
	Toxic
	Vincristine induced
Inherited	Organophosphate poisoning
22q11 microdeletion	Metabolic
Robinow syndrome	Hypokalemia

Unlike adults, congenital BVFMI is most commonly related to an underlying central nervous system (CNS) disorder. The most common CNS abnormality contributing to bilateral vocal fold paralysis is an Arnold-Chiari malformation [9]. Central neural degenerative disease including syringomyelia and syringobulbia is also associated with BVFMI [10, 11]. Additional CNS causes of vocal fold immobility include leukodystrophy, encephalocele, hydrocephalus, and cerebral or nuclear dysgenesis [12, 13]. Peripheral disorders such as congenital myasthenia gravis have also been implicated in congenital BVFMI although this is much more likely to occur in older children and adults [14, 15].

Similar to adults, surgical trauma in children can contribute to vocal fold immobility. Any procedure with close proximity to the recurrent laryngeal nerve has the added risk of vocal fold paralysis. Surgical trauma in infants generally results in unilateral immobility, but patients undergoing tracheoesophageal fistula (TEF) repair, especially H-type TEF, are at risk of developing bilateral vocal fold immobility [16]. Blunt trauma resulting in closed head injuries, especially involving the posterior fossa, can also contribute to bilateral vocal fold immobility [17].

Metabolic and toxic etiologies should also be considered in the differential for BVFMI. Bilateral vocal fold immobility has been associated with hypokalemia as well as organophosphate poisoning [18, 19]. Additionally, vocal fold immobility, both unilateral and bilateral, has been described as an adverse effect of vincristine with a dose-related response that resolves slowly after discontinuation of the medication [20].

Although rare, a variety of genetic syndromes associated with familial vocal fold paralysis have been described [21–24]. Hsu et al. reviewed the literature and found a number of genetic syndromes associated with bilateral neonatal and adult onset vocal fold immobility. Most notably a specific balanced translocation between chromosomes 5 and 14 is associated with an autosomal dominant inheritance of neonatal BVFMI [25]. A separate report of 21 cases of familial BVFMI identified a variety of inheritance patterns including autosomal dominant, X-linked dominant, and X-linked recessive [24]. Additionally, conditions such as 22q11 deletion or Robinow syndromes have also been associated with congenital BVFMI [26].

Bilateral vocal fold immobility has also been associated with inflammatory conditions related to underlying infections and granulomatous diseases. There are reports of patients infected with polio, tuberculosis, cytomegalovirus, West Nile virus, and herpes simplex virus presenting with bilateral vocal fold immobility [27–31]. Although Guillain-Barré syndrome rarely affects laryngeal function, it has been associated with bilateral vocal fold immobility when laryngeal function is compromised [6, 32].

Presentation and Diagnostic Evaluation

The most common manifestation of bilateral vocal fold paralysis is stridor [6]. These patients typically present with respiratory distress [33••]. In addition to considerable airway obstruction, BVFMI presents with symptoms common in unilateral vocal fold immobility such as ineffective cough, aspiration, recurrent pneumonia, reactive airway disease, and feeding difficulties [34••, 35]. Voice and cry may be fairly normal in children with BVFMI [36]. In a study by Jabbour examining 102 pediatric patients with BVFMI, 40% presented with dysphagia, and 51% required a gastrostomy tube [37].

Diagnosis is made by performing a thorough history and physical exam. First, a proper description of the effort of breathing including stridor should be completed. Second, speech and swallowing difficulties are evaluated. Any history of prior intubation or other surgical interventions should be documented. Associated medical conditions or congenital anomalies, such as neurologic disorders or congenital heart disease, must be investigated. Early diagnosis can be made by fiberoptic examination of the larynx, but a significant proportion of the children will need immediate intubation after birth due to intense respiratory distress [38]. Therefore, evaluation of the airway may require examination under general anesthesia with spontaneous ventilation [39]. Microlaryngoscopy should consist of visual inspection as well as palpation of the arytenoid to rule out cricoarytenoid fixation and close evaluation of the posterior glottis to rule out stenosis. Grading of the posterior glottic stenosis can be performed using the Bogdasarian classification [40]. Diagnosis can occasionally require laryngeal EMG. If volitional activity is present, late spontaneous recovery is possible and can be anticipated [41••].

Management

Management of BVFMI requires a multidisciplinary approach including intensivists, skilled otolaryngologists, and speech-language pathologists. The primary treatment is to provide a safe airway that does not compromise the patient's life. The main decision is the need for tracheotomy. On average 19.2–74% of BVFMI patients will require a surgical airway [37, 38, 42, 43]. However, some small case series describe a 0% need for tracheotomy [44, 45], and other small series show a 90–100% need for a tracheotomy [13, 41••]. This range reflects much variation in provider's management of BVFMI.

Improvements in neonatal care, the assessment and monitoring of apnea, and use of nasal CPAP or high-flow air by nasal cannula may be helpful in decreasing the need for tracheotomies in children. These tools might help providers “buy time” since spontaneous

recovery has been shown to occur in 50–65% of pediatric patients [38, 42, 43]. This recovery can occur in as little as 5 months to more than 3 years after the initial diagnosis or birth [46, 47]. However, if patients are unable to remain extubated, then a tracheotomy may be warranted [38].

The evaluation of BVFMI usually involves neurological assessment, imaging studies [48], and swallowing studies [49]. Oral feeding can exacerbate obstruction and airway symptoms in these patients. A nasogastric (NG) tube can help relieve these symptoms; one study reported 73% of BVFMI require NG tube feeding [38]. Gastrostomy tube feedings can also be necessary to relieve patients from the need of prolonged NG feeding. Jabbour and colleagues showed that 51% of patients with BVFMI required insertion of gastrostomy tubes [37].

Many centers believe that after 1 year, a chance for spontaneous recovery is low, and a procedure that can help decannulation should be offered [45, 46, 50]. Other centers recommend waiting several years, for possible spontaneous recovery, before an irreversible procedure is attempted [16, 39]. Berkowitz suggested that patients with congenital BVFMI can have spontaneous recovery in their second quinquennium of life and can eventually be decannulated if they have a tracheostomy in place [47]. This might also depend on the etiology of injury with higher rate of spontaneous recovery in central neurologic injury and lowest rate in iatrogenic injuries [46]. A study on 102 patients by Funk showed that idiopathic causes for BVFMI demonstrated higher rates of resolution compared to patients with a neurogenic etiology (46.7% vs 14.3%) [51].

Patients that cannot be decannulated and who do not have spontaneous resolution of VFP have several options to have an improved airway patency. These options are divided into “static”, “chemical”, and “dynamic” approaches. Static procedures involve laryngeal framework surgery either by resection of tissue [33••, 52–54, 55••]. Laryngeal chemodenerivation, another form of managing BVFMI, is performed by targeting the thyroarytenoid muscle [56] or the cricothyroid muscle using botulinum A injections [57]. Dynamic procedures include laryngeal reanimation procedures (e.g., reinnervation) and functional electrical stimulation.

Static Procedures

Static procedures improve airway patency by enlarging the glottic aperture. This can be accomplished either by excising laryngeal tissue, fixation techniques, or enlargement of glottic circumferential area. Multiple procedures can be employed simultaneously. The expected consequence of static procedures is a decline in voice quality in volume and roughness of the voice in a compromise for a larger glottic airway.

Cordotomy

Cordotomy with or without arytenoidectomy has been described in adults from 1983 using the carbon dioxide (CO₂) laser [58]. Children have a smaller larynx, where the balance between voice and airway patency is very delicate and harder to predict. Cordotomy has been described in children with high success regarding airway, but voice outcomes have not been prospectively assessed. The procedure consists of an incision in the posterior third of the true vocal fold laterally to the thyroid cartilage [59]. Studies demonstrated 89 to 100% of patients treated with cordotomy were ultimately decannulated or avoided tracheotomy altogether [59, 60]. However, some patients require multiple revisions due to persistent symptoms of dyspnea. The voice is expected to be adversely affected; however, the degree of dysphonia and the effect on quality of life have not been prospectively addressed.

Arytenoidectomy

Endoscopic laser arytenoidectomy is another alternative and has a similarly high rate of success. The procedure consists of vaporization of the medial part of the arytenoid with preservation of the posterior-lateral mucosal wall [61]. In a study by Aubrey, 75% of patients were able to be decannulated at a mean of 2 months postoperatively. One of these patients required a cordotomy for recurrence of dyspnea. Out of the 17 patients treated, 5 had postoperative dyspnea, 3 improved with voice therapy, and 2 required vocal fold augmentation [61]. Another study showed success in treating 6 patients with arytenoidectomy without postoperative speech impairment [62].

Arytenoid Lateralization

Endoscopic percutaneous suture lateralization for bilateral vocal fold immobility has also been described in the literature and is recently gaining popularity especially in neonatal BVFMI [63]. Multiple methods can be used to perform this procedure including the use of ultrasound to guide suture placement [64]. Sztanó and colleagues demonstrated a 3/3 success rate with a greater than 3-year follow-up [65••]. Montague had a 5/5 success rate after excluding 1 patient that expired due to seizures. However, 1 patient had aspiration and had resolution of symptoms after suture removal [66].

Endoscopic Anterior-Posterior Cricoid Split

Another static method to enlarge the airway is the endoscopic anterior-posterior cricoid split. In this method, the posterior cricoid is incised first using a laryngeal knife or CO₂ laser. The anterior cricoid is then incised through a mucosal incision

made with a sharp sickle knife while exercising caution to avoid injury to the anterior commissure [33••]. Rutter demonstrated a 74% success rate overall with only 3 of 19 patients requiring tracheotomy following anterior-posterior cricoid split. Another more recent study on 6 patients showed a 50% success with the rest of the patients requiring tracheotomy [55••]. The procedure was reported to “not affect the voice” [33••] though voice outcomes were not measured or documented in either study.

Posterior Cricoid Cartilage Graft

Posterior cricoid cartilage graft has been performed for BVFMI by widening the posterior glottis [67]. A rib cartilage is harvested, carved, and placed in position after performing a posterior cricoid. This procedure has mixed results overall. A few studies demonstrated that 100% of patients were either decannulated or were able to avoid a tracheotomy [67–69]. In contrast, a study by Dahl showed a 2/7 rate of decannulation in patients with BVFMI [70••]. However, Dahl argues that this low rate of decannulation could be due to the possibility that each institution might have different protocols for decannulation [70••]. The potential for adverse voice outcomes after posterior cricoid graft laryngoplasty has documented from numerous retrospective studies. A breathy weak voice ensues from posterior glottis incompetence when the graft displaces the arytenoids too widely. Compensatory supraglottal phonation may develop. Cricoid reduction laryngoplasty to remediate this problem has been recently reported. [71]

Laryngeal Chemodeneration

Cohen first described the use of botulinum toxin for treatment of BVFMI in a canine model in the 1980s. Injection of the cricothyroid muscle was found to relax the tension of the true vocal fold resulting in lateralization with improvement of airway obstruction [57, 72]. Smith et al. later described the use of botulinum toxin injections to the thyroarytenoid muscle to treat 10 pediatric patients with BVFMI. In this study, 4 patients experienced improvement in airway obstruction sufficient enough to either avoid tracheostomy or facilitate decannulation. Of the 6 patients with no improvement, four had significant central nervous system comorbidities [73].

A more recent study described injection of onabotulinum toxin A into the cricothyroid muscle of 6 pediatric patients with BVFMI. All patients experienced improvement in airway obstruction within days of injection. Five patients avoided tracheostomy, and the 6th was successfully following treatment [74].

Lewis and Woo also described their experience using botulinum toxin injection in patients with BVFMI and underlying laryngeal synkinesis following iatrogenic injury [75••]. After

injection of the TA and/or PCA, 5 of 8 patients experienced adequate improvement in dyspnea. Two patients were successfully decannulated following injections. Overall, botulinum toxin injection appears to be less effective than other treatments but can certainly provide benefit in appropriately selected patients. The obvious downside of this treatment option is the need for repeat injections to maintain results.

Reanimation Techniques

Laryngeal Reinnervation

While static procedures are successful approaches to managing the airway and ultimately can help with decannulation in patients with BVFMI, these procedures often result in worsening phonation and increased aspiration. In contrast, laryngeal reinnervation provides an alternative approach with the goal of improving both abduction and adduction of the bilateral vocal folds. Additionally, these procedures have the added benefit of being entirely extralaryngeal so there are no mucosal incision or changes to the laryngeal framework ultimately limiting the risk of laryngeal scarring and/or intraluminal granulation formation.

During the 1970s and 1980s, Tucker studied laryngeal reinnervation by ansa cervicalis nerve-muscle pedicle transfer to the posterior cricoarytenoid muscle in 202 patients with BVFMI. He reported long-term success in 74% of patients undergoing the procedure although only 50% of tracheostomy dependent children were ultimately decannulated [76, 77]. In 1998, Zheng et al. demonstrated in a canine model superior outcomes in reinnervation with the nerve suture technique (compared with direct nerve implant into muscle and nerve-muscle pedicle) in which the nerve graft is approximated to the adductor branch of the RLN using an epineural stitch with 11–0 nylon suture [78].

After several experiments, J.P. Marie developed a procedure consisting of bilateral selective reinnervation of the adductor and abductor muscles of the larynx [79]. From these, the necessity to use phrenic nerve roots to drive reinnervated inspiratory muscles was documented [80]. The paralyzed posterior cricoarytenoid (PCA) abductor muscles are reinnervated by grafting with the greater auricular nerve (GAN) Y-graft from a rootlet of the phrenic nerve directly implanting to each lateral PCA belly. The adductor muscles of the larynx on each side are reinnervated by the thyrohyoid nerve via a GAN jump graft and connected to the main RLN trunk. To date, long-term follow-up has been achieved in more than 80 adult patients, since 2013 (JP Marie, unpublished results). A recent study by Lee, Mardion, Smith, and Marie demonstrated promising outcomes in 8 pediatric patients with bilateral vocal fold paralysis [34••]. The median age at time of reinnervation was approximately 9 years. Six of the eight patients required preoperative tracheostomy for airway management. Long-term

follow-up demonstrated decannulation of all patients with an average time to decannulation of just under 1 year after surgery. Vocal fold abduction on inspiration was observed in 7 patients, and the 8th patient demonstrated clinical improvement in respiratory function although no visible movement was noted on flexible laryngoscopy [34••]. This study demonstrates great promise for treatment of BVFMI with selective laryngeal reinnervation.

A group in China described success with a similar selective laryngeal reinnervation technique [81••]. The operation entails dissecting out the damaged RLNs and grafting the upper root of the right phrenic nerve to the common trunk of the RLN bilaterally. The branch to the interarytenoid muscle on each side is divided. Next, the thyroid branch of the hypoglossal nerve is anastomosed to the adductor branches of the RLNs on both sides. The group reported results on 7 patients with BVFMI post-thyroidectomy confirmed by EMG. In 6 of the 7 patients, there was return of function to both vocal folds, and at least one vocal fold demonstrated moderate to maximal movement. The 7th patient exhibited no movement on one side and minimal movement on the contralateral side. PFTs were also significantly improved and within the normal reference values 3 months after surgery.

Laryngeal Pacing

Given the previous success with implantable devices such as cardiac pacemakers, cochlear implants, and even hypoglossal nerve stimulators, recent studies have investigated the use of implantable devices in laryngeal pacing for treatment of BVFMI. In this surgery, the device electrode is implanted into the PCA muscle, and stimulation of abduction is confirmed intraoperatively. The implantable device is then placed in a subcutaneous pocket overlying the sternum [82••, 83]. A study by Zeale and colleagues evaluated 7 patients who underwent implantation of a laryngeal pacing device. Five patients had significant improvement particularly in their peak inspiratory flow measures at follow-up. Four patients met criteria for decannulation. Of the 2 failures, 1 patient had an infection of the implant requiring removal, and the other did not exhibit stimulated abduction after surgery [83]. More recently, Mueller reported results of a different implantable device in 9 adult patients with BVFMI [82••]. Of the 7 adult patients completing the study, a significant improvement in peak inspiratory and peak expiratory function was noted. There was no change in voice or swallowing parameters.

Although initial outcomes of laryngeal pacing are promising, there are a few notable disadvantages. First, the surgery requires an implantable device with the possibility of infection, extrusion, and failure. Second, the device does not have an inspiratory sensor and is not synchronized with the patient's inspiratory effort. Programming is possible, but ultimately the patient must learn to adjust their respiratory rate

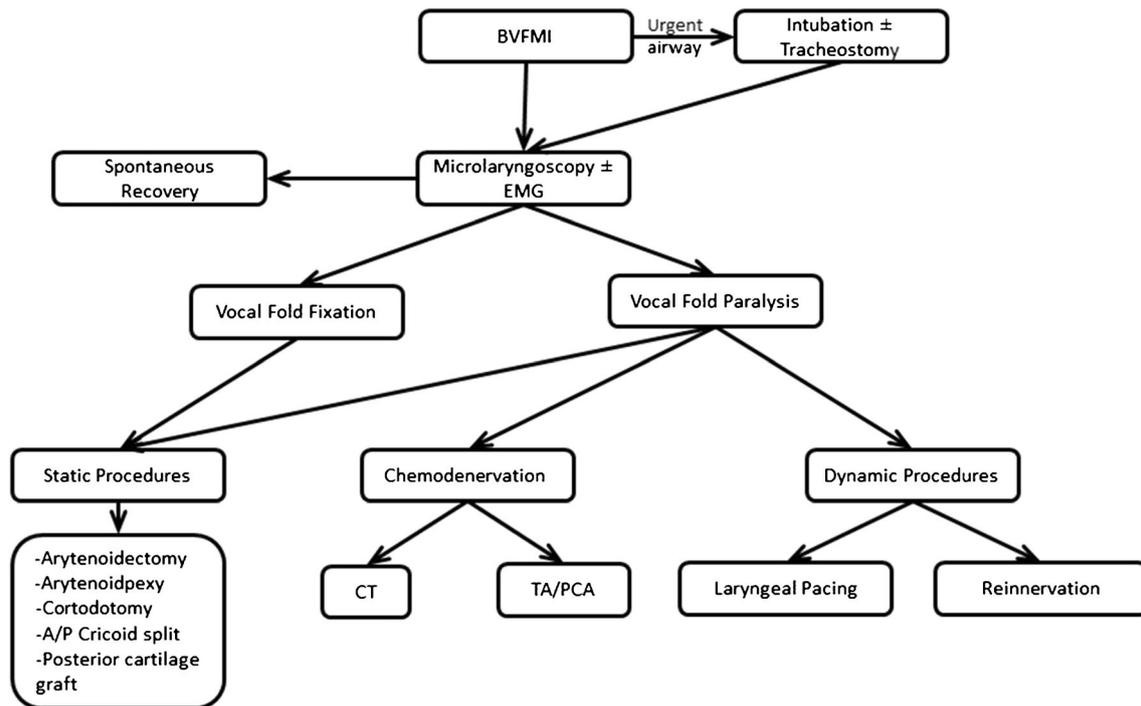


Fig. 1 Algorithm for the approach bilateral vocal fold mobility impairment. BVFMI (bilateral vocal fold mobility impairment), EMG (electromyography), A/P (anterior/posterior), CT (cricothyroid), TA (thyroarytenoid), PCA (posterior cricoarytenoid)

to the programmed stimulus cycle [82•, 83]. Regardless, this approach shows considerable promise and will likely continue to improve with technological advances.

Conclusion (Figure 1)

BVFMI is a life-threatening disease especially in the pediatric population. Although a thorough history and physical exam are crucial in arriving at the appropriate diagnosis, securing the airway is the primary goal of the caring team. A multidisciplinary approach is vital in the long-term course of this disease. Breathing, swallowing, and speech are the three pillars that need to be balanced in order to improve the quality of life of the patients.

Treatment should be tailored according to each patient but also to the experience of the otorhinolaryngologist. As patients may experience spontaneous recovery, a trial of conservative treatment can be planned initially. When conservative measures fail, static procedures that are less vocally impairing or chemodeneration procedures can be tried. Additionally, some patients might require multiple procedures. Dynamic interventions provide promising alternatives to tracheostomy and static procedure. At this time, laryngeal reinnervation (in children and adults) and laryngeal pacing (in adults) provide excellent alternatives to more traditional techniques. When it is apparent that a surgical procedure with long-term

improvement in airway is necessary, we first consider if the patient is a candidate for bilateral selective reinnervation. If not, or if laryngeal reinnervation is unsuccessful, then a long-term static procedure can be employed, such as a posterior cricoid cartilage graft. With continued research and further advances, the reinnervation and pacing approaches might be the preferred treatment options with the ability to optimize the 3 pillars of laryngeal function.

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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