Injection Laryngoplasty for Children with Unilateral Vocal Fold Paralysis: Procedural Limitations and Swallow Outcomes

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Abstract

Objective. Vocal fold immobility with resultant dysphagia is a known cause of morbidity in the pediatric population. Herein we evaluate the efficacy and adverse events of injection laryngoplasty in children.

Study Design. Case series with chart review.

Setting. Tertiary academic children’s hospital.

Subjects and Methods. Patients <12 years of age with unilateral vocal fold immobility, dysphagia, and objective swallow study data were included. Primary outcome measures included perioperative adverse events and the ability to advance the diet, as defined by initiation of oral feeds or reduction in thickener following postoperative swallow study.

Results. The mean age of the cohort (N = 41) was 43.83 months (range, 0.5-144 months), and 46.3% of patients were <18 months old. Perioperative adverse events included increased oxygen requirement (n = 3), prolonged operating room time secondary to tenuous cardiopulmonary status (n = 2), and postoperative readmission within 30 days (n = 1). A total of 63.63% (n = 21 of 33) of patients safely advanced their diet following objective improvement on swallow study. Patients undergoing injection laryngoplasty ≤6 months of the onset of vocal fold immobility were more likely to advance their diet following surgery.

Conclusion. Injection laryngoplasty has the potential to advance or initiate an oral diet for children with vocal fold immobility, including those in the first months of life. It is relatively free of adverse events, but certain limitations in the pediatric population must be considered. Preoperative characteristics, including timing of injection and premorbidity diet, may guide clinicians in predicting those patients most likely to advance their diet following injection laryngoplasty.

Keywords
dysphagia, swallow, dysphonia, pediatrics, vocal fold paralysis, injection laryngoplasty, medialization

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Unilateral vocal fold immobility (UVFI) is a known cause of morbidity in the pediatric population, especially among children having undergone congenital heart surgery or following prolonged intubation. Glottal incompetence and laryngeal dysfunction can result in abnormal swallow function, inadequate cough, increased risk of silent aspiration, and dysphonia.¹² Following recurrent laryngeal nerve injury, an often-unpredictable degree of recovery of laryngeal function will ensue in the next several months, with recovery cited to occur >18 months after insult. The range of recovery rates in the existing literature is variable, ranging from <20% for some data regarding iatrogenic injury during cardiothoracic surgery to >70% among cohorts of idiopathic cases.¹-⁴ Injection laryngoplasty (IL) can be a temporary intervention that allows for improved symptoms during the window of potential recovery without permanent adverse effects.

An objective risk-benefit profile of IL is well documented in the adult literature, but pediatric cohorts are small and heterogeneous, particularly the prepubertal and very young patient cohorts.⁵-⁷ Herein we evaluate the effectiveness and procedural limitations of IL in the pediatric population, with a proportionally large subset of children in the first 18 months of life. To our knowledge, this is the first study beyond a case series to use objective swallowing data.
as an outcome measure for pediatric patients undergoing IL for UVFI.

**Materials and Methods**

The study (case series with chart review) was approved by the institutional review board of Lucile Packard Children’s Hospital (LPCH) Stanford. The project described in this publication was supported by the Stanford Child Health Research Institute; assistance with Institutional Review Board applications and data management was provided. Data were collected through the LPCH Stanford Medicine Research Data Repository and augmented with a chart analysis to completely characterize the cohort. The database searches were by *Current Procedural Terminology* code and *International Classification of Diseases* code; both strategies were used and cross-referenced. All pediatric patients who underwent IL for UVFI between February 1, 2006, and February 6, 2018, were initially evaluated. In an effort to isolate young patients with available objective swallowing data, only patients with unilateral vocal fold dysfunction, age <12 years, and pre- and postoperative swallow studies were selected for further review. Two patients were excluded because they underwent vocal fold injection for chronic aspiration in the setting of tracheostomy dependence. The majority of exclusions were otherwise secondary to unavailable pre- or postintervention swallow study data.

The onset date of vocal fold immobility and/or injury to the recurrent laryngeal nerve was extracted from the medical record (eg, if the etiology was presumed to be iatrogenic following cardiothoracic surgery, then the date of injury was listed as the date of cardiac surgery). If the origin was congenital, the date of birth was used as the onset date. The diagnosis of UVFI was made by flexible laryngoscopy performed and/or interpreted by an attending pediatric otolaryngologist. To clarify, the date of presumed onset based on etiology was used as the date of onset for the diagnosis of UVFI, not the date of flexible laryngoscopy. All patients received a clinical swallow evaluation by an occupational therapist and/or speech-language pathologist who specializes in the evaluation and treatment of feeding and swallowing dysfunction among children. Patients underwent at least 1 pre- and postprocedural instrumental swallow study at LPCH (ie, fiberoptic endoscopic evaluation of swallowing and/or videofluoroscopic swallow study). Postintervention swallow studies were performed between 5 and 15 days following IL. All patients had persistent vocal fold immobility documented by laryngoscopy at the time of the postoperative swallow evaluation.

Patients were stratified into binary cohorts based on the time from presumed insult (eg, date of cardiac surgery) to the date of the initial IL procedure, either ≤6 or >6 months. Pre- and postinjection instrumental swallow studies were interpreted by a senior speech-language pathologist, occupational therapist, or otolaryngologist (D.R.S.) as applicable. If patients underwent multiple vocal fold injections, only the first injection was evaluated in this study. Premorbidity diet was determined by the oral intake prior to the presumed time of vocal fold insult. If a patient received both oral and tube feeds, the method of intake for >50% of calories was used to determine the premorbidity diet.

All patients underwent IL via transoral suspension microlaryngoscopy under general anesthesia. With 1 exception, all patients underwent IL with spontaneous ventilation; 1 patient was intubated for the procedure. A mean 0.23 mL of a temporary substance was injected (range, 0.1-0.55 mL; 95% CI, 0.20-0.27 mL). For patients <2 years of age, the vocal fold is typically overcorrected by <20% or just to the midline. All patients ≤2 years of age were injected by a single surgeon, with infrequent involvement of a single pediatric otolaryngology fellow (n = 3). Older patients were injected by either an attending pediatric otolaryngologist or a senior-level trainee. The most frequently used initial injection material was sodium carboxymethylcellulose (Prolaryn Gel; Merz North America), which was used for 85.4% of the patients (n = 35). Other injectables included calcium hydroxylapatite and Cymetra; no autologous fat was used. Carboxymethylcellulose was used exclusively for the first injection of children <24 months.

Primary outcome measures include the ability to advance the oral diet following injection and the presence or absence of perioperative adverse events. Liberalization of the diet was defined as improvement in diet following injection, specifically characterized by the initiation of oral feeds or a decrease in thickener requirement postoperatively. At this institution, perioperative diet is based on the risk of aspiration present on instrumental swallow study. All patients who advanced or improved diet following injection in this study had improved swallow function and a reduced risk of aspiration visible on instrumental swallow study postoperatively.

Minor adverse events included temporary changes in condition requiring minor intervention (eg, postoperative oxygen, prolonged operative time) and lasting <24 hours. Major adverse events were classified as those requiring major intervention (eg, intubation, readmission) or lasting >24 hours.

Descriptive statistics were used to summarize patient demographics, premorbidity diet, etiology of UVFI, and other descriptors. For continuous data, mean, range, and 95% CI were used to provide descriptive statistics. Two-tailed Fisher’s exact test at a significance level of *P* < .05 was used to investigate categorical data, such as comparing swallowing outcomes of patients ≤6 and >6 months after injury, given the relatively small sample sizes. Statistical analysis was performed on GraphPad Prism 7.0 (GraphPad, La Jolla, California).

**Results**

**Patient Demographics and Perioperative Complications**

Of the 108 children who underwent vocal fold IL, 41 met inclusion criteria, of whom 51.2% were female. The mean age of the cohort (n = 41) was 43.83 months (range, 2 weeks–12 years; 95% CI, 30.05–57.61 months), and 46.3% of patients were <18 months of age. The minimum weight was determined by the oral intake prior to the presumed time of vocal fold insult. If a patient received both oral and tube feeds, the method of intake for >50% of calories was used to determine the premorbidity diet.

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for injection was 2.5 kg. For 35 patients, the presumed etiology of UFVI was iatrogenic following cardiac surgery (ranging from patent ductus arteriosus ligation to complex reconstruction of the aortic arch) or extracorporeal membrane oxygenation cannulation. Other causes included congenital (n = 2), traumatic following blunt neck trauma (n = 1), neurologic (n = 1), and intubation related (n = 2). The mean time elapsed between the presumed date of injury to first vocal fold injection was 21.87 months (range, 10 days–9.7 years; 95% CI, 11.8-31.95 months). IL was performed ≤6 months after presumed injury for 21 patients (51.22%). Of 41 patients, 14 (34.1%) ultimately underwent >1 injection. These patient characteristics are summarized in Table 1.

Adverse events were extracted surrounding the initial IL procedure only. Minor perioperative adverse events included increased oxygen requirement postoperatively (n = 1), prolonged operative time secondary to tenuous cardiopulmonary status (n = 3), and intraoperative laryngospasm (n = 1). Major events included need for intubation 2 days following injection (n = 1) and postoperative readmission within 30 days due to symptoms consistent with upper respiratory infection (n = 1). The patient who required postoperative readmission was also included in the minor event group for prolonged operative time secondary to tenuous cardiopulmonary status. In total, the minor complication rate was 12.2% (5 of 41), and the major complication rate was 4.88% (2 of 41). The minor adverse events were thought to be related to difficulty in maintaining spontaneous ventilation in the setting of delicate cardiopulmonary status, as all patients had either severe bronchopulmonary dysplasia or congenital heart disease. The incidence of minor adverse events did not have any specific pattern that could be attributed to patient age (soft surrogate for airway size) or surgeon experience. At least 1 patient likely had a previously unrecognized viral respiratory illness, which led to prolonged operative time and need for readmission within 30 days. The 2 major adverse events did occur in the winter months and were both thought to occur with concurrent upper respiratory infection. The patient requiring reintubation was extubated without incident. However, this patient did not undergo repeat injection and did not show an improved swallow. The patient readmitted within 30 days was maintained with noninvasive ventilation but did not show an improved swallow postoperatively. These are summarized in Table 2.

Swallowing Outcomes

Three patients were excluded from secondary analysis of swallowing outcomes due to incomplete data generated during the swallow study (eg, severe oral aversion complicating results) or during the subsequent clinic visit (eg, no caregiver was available to confirm the patient’s current diet). Of the 38 remaining patients with complete data, 5 were tolerating an age-appropriate diet without a need for modification and underwent injection to improve dysphonia. All 5 patients maintained an age-appropriate diet postoperatively. Thirty-three patients had evidence of dysphagia characterized by aspiration on thin liquids on instrumental swallow study prior to injection. A total of 63.63% (n = 21 of 33) of patients were able to advance their oral diet following objective improvement on instrumental swallow study following injection. The increased oral intake resulted from changes such as going from nothing by mouth to oral feeds or transitioning from thickened feeds (eg, honey thickened) to a thinner consistency (eg, thin or nectar) with a resultant increase in total oral consumption. As shown in Figure 1, a larger proportion of patients undergoing IL within 6 months (vs >6 months) of the presumed vocal fold insult were recommended an advanced diet (75% vs 35.71%, P = .035; odds ratio, 5.4; 95% CI, 1.12-20.42).

As demonstrated in Figure 2, advancement of diet after IL occurred more often for patients who tolerated an age-appropriate oral diet prior to the onset of vocal fold immobility versus those who required other feeding strategies (eg, use of thickener) or supplemental means of nutrition (eg, nasogastric tube feeds) (55% vs 14.3%, P = .030; odds ratio, 7.33; 95% CI, 1.20-37.37).

Discussion

Based on the data presented here, IL in children, including those in the first 18 months of life, appears to have a low rate of complications. Moreover, it has the potential to improve the swallow outcomes of the majority of patients at our institution. In this review, 1 patient required intubation due to increased work of breathing on postoperative day 2. This intubation was thought to be unrelated to the vocal fold injection and instead due to viral upper respiratory infection in the setting of congenital cardiac disease and bronchopulmonary dysplasia. The second major complication, readmission, was also attributed to viral upper respiratory infection. Although the 2 major complications were thought to be unrelated to the IL procedure, the benefits of the intervention itself must be weighed heavily against any potential perioperative risks. At our institution, all patients with a history of cardiopulmonary disease are reviewed by cardiology and cardiac anesthesiology prior to undergoing intraoperative IL.

Table 1. Patient Characteristics.

<table>
<thead>
<tr>
<th>Patient Variable</th>
<th>Patients, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mo</td>
<td>43.83 (2 wk–12 y)</td>
</tr>
<tr>
<td>&lt;18 mo</td>
<td>19 (46.3)</td>
</tr>
<tr>
<td>Presumed etiology</td>
<td></td>
</tr>
<tr>
<td>Iatrogenic</td>
<td>35 (85.4)</td>
</tr>
<tr>
<td>Congenital</td>
<td>2 (4.9)</td>
</tr>
<tr>
<td>Blunt neck trauma</td>
<td>1 (2.4)</td>
</tr>
<tr>
<td>Neurologic</td>
<td>1 (2.4)</td>
</tr>
<tr>
<td>Intubation related</td>
<td>2 (4.9)</td>
</tr>
<tr>
<td>Time between injury to injection, mo</td>
<td>21.87 (10 d–9.7 y)</td>
</tr>
<tr>
<td>≤6 mo elapsed</td>
<td>21 (51.2)</td>
</tr>
</tbody>
</table>

*Forty-one total patients, of whom 38 had complete objective swallowing data.

bMean (range).
This warrants a thorough assessment by all services involved in the patient’s care and a comprehensive discussion with the parents of the child, detailing the risks and perceived benefits of this procedure. Nevertheless, our data support the recent best practice statement by the Triological Society suggesting that temporary injection may improve the morbidity of patients with UVFI during the waiting period with little risk of perioperative complications.8

The adult literature has proposed that patients undergoing medialization procedures soon after insult may have improved long-term swallowing outcomes beyond the expected duration of the injected agent.9-12 Friedman et al reported that patients receiving an early injection (<6 months from diagnosis of immobility) versus a late injection were less likely to require laryngeal framework surgery.13 The authors proposed that the more medialized position of the true vocal fold promotes favorable synkinesis.13 It may also be that the trauma and inflammation induced by the injection change the milieu of the reparative state in a way that is favorable to neural reinnervation. Alternatively, those patients undergoing early IL may be less likely to develop compensatory strategies that are counterproductive to an effective swallow. Currently, there is no literature on any of these phenomena in the pediatric population. Although the mechanism is not understood with certainty, our data also support the perceived benefit of early IL (<6 months) for UVFI in the pediatric population in consideration of swallowing outcomes.

### Table 2. Perioperative Complications Following Injection Laryngoplasty.

<table>
<thead>
<tr>
<th>Age, mo</th>
<th>Weight, kg</th>
<th>Comorbidities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Need for increased oxygen</td>
<td>3.9</td>
<td>3.74</td>
</tr>
<tr>
<td>Prolonged operative time</td>
<td>114</td>
<td>24.5</td>
</tr>
<tr>
<td></td>
<td>11.87</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>7.4</td>
<td>6.75</td>
</tr>
<tr>
<td>Laryngospasm</td>
<td>1.3</td>
<td>2.6</td>
</tr>
<tr>
<td>Major</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Postoperative intubation at 30 h</td>
<td>61.3</td>
<td>15.7</td>
</tr>
<tr>
<td>Readmission within 30 d</td>
<td>7.4</td>
<td>6.75</td>
</tr>
</tbody>
</table>

Abbreviations: CHD, congenital heart disease; CLD, chronic lung disease; GA, gestational age; OSA, obstructive sleep apnea.

*Figure 1. Advancement of diet among patients undergoing injection laryngoplasty ≤6 months of presumed vocal fold insult versus >6 months. *P < .05.

*Figure 2. Advancement of diet among patients with an age-appropriate baseline diet versus patients who needed an alternative diet (eg, thickener or tube feeds). *P < .05. IL, injection laryngoplasty; PO, per os.*
Tibbetts and colleagues recently reported the recovery of vocal fold mobility and recovery of swallowing function among pediatric patients. Their data suggest that the recovery of swallowing function surpassed rates of return of motion. Conversely, there were also patients with recovery in vocal fold mobility but without recovery of swallowing in that study.¹⁴ In this report, procedural “success” was more commonly attributed to achieving our primary goal—namely, to reduce the risk of aspiration visible on instrumental swallow study. Thus, following injection, if we were able to (1) provide an oral diet to patients for whom oral feeds were previously unsafe or (2) thin the consistency of oral liquids for patients with an augmented diet, we considered our intervention successful.

Other factors—including prolonged recovery periods following cardiac surgery, prolonged periods of postoperative intubation, and general comorbidities—likely play a role in the recovery of swallow function for certain patients. Likewise, and despite the objective nature of instrumental swallow evaluations performed herein, interpretation of the swallow evaluation of patients with cardiopulmonary comorbidities and a low tolerance of aspiration events may err cautiously toward documenting residual swallow dysfunction. Swallowing and phonating are complex mechanisms that span beyond the location, movement, and bulk of the vocal folds. Our general practice is to reevaluate swallowing with a focused instrumental swallow study after IL, regardless of the clinical and subjective voice outcomes.

It is not surprising that those patients with an age-appropriate premorbidity diet were more likely to have liberalization of diet after IL. Swallow function is often more likely to return to baseline when patients present with a normal swallow prior to any insult on feeding and swallowing. This directly reflects the complexity of swallow function, including coordination, timing, and strength of the swallow. When other elements of swallow function are intact, the patient is often more capable of compensating for larynx are unknown.

Despite the strengths of this investigation, several shortcomings merit mention. Foremost, this study bears those limitations inherent to a case series with chart review. Other limitations include the barriers surrounding objective outcomes and validated instruments related to voice, swallowing, and quality of life in the pediatric population. Patient cooperation with instrumental swallow studies can be unpredictable and inconsistent among studies as well as individuals. In addition, the preinjury diet of this patient group was variable, with some having dysphagia prior to the onset of vocal fold immobility and others demonstrating appropriate swallow function based on clinical history and/or instrumental studies. There is also an unknown burden of dysphagia among children undergoing congenital heart surgery without UVFI. Overall, the natural course of this patient cohort is largely unknown, and it is impossible to know the incremental dysfunction caused by vocal fold immobility among those children with preexisting complex dysphagia. Last, the sample size of the present cohort is small, and there is potential for selection bias, limiting the ability to make conclusions and calculate more sophisticated statistics.

Several practical limitations to performing IL in children exist. These include the comparatively large size of the injection needle given the small vocal fold and paraglottic space, particularly during infancy. This mandates adequate exposure, surgical accuracy, and an experienced operator. Anatomic differences among the infant, child, and adolescent lamina propria may also make injection results less predictable.¹⁵ Furthermore, because of the size of the glottic aperture, there is less tolerance for overinjection, particularly with longer-lasting implant materials or with repeat injection. Special considerations of the pediatric population also include the requirement for general anesthesia when IL is performed, a relatively high incidence of aerodigestive and cardiopulmonary comorbidities, and difficulty in quantifying swallowing and voice outcomes homogeneously. Last, while occupational therapy and/or speech-language pathology is invariably involved in the treatment of patients with swallow dysfunction at our institution, a specific protocol was not followed for all patients in this study. Thus, the role of swallowing therapy, either as a first-line therapy or as an adjunct to IL, is difficult to characterize in this patient population. While swallowing therapy is well defined as a resource in the adult literature, the utility is controversial and often provider specific, particularly for children <2 to 4 years of age. Therefore, we assume that the children in this cohort may have had variable exposure to speech and swallowing therapy within our institution and potentially beyond.

**Conclusion**

IL is a procedure performed relatively free of adverse events, and it has the potential to improve the swallow function of young pediatric patients with UVFI, including those in the first months of life. In this study, postoperative improvement was primarily associated with a reduced risk of aspiration on swallow study and the ability to provide an
advanced diet as a result. This appeared most consistent for the patients undergoing IL ≤ 6 months of presumed date of UVFI. Preoperative swallow study characteristics suggestive of isolated glottic incompetence and otherwise coordinated swallow function may guide clinicians in predicting those patients who are most likely to liberalize their diet following IL, as patients with more comorbidities are more likely to have global swallow dysfunction.16

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Author Contributions
Kara D. Meister, conception and design, acquisition of data, analysis and interpretation of data; drafting the manuscript; revision of manuscript; final approval; April Johnson, acquisition of data, analysis and interpretation of data; revision of manuscript; final approval; Douglas R. Sidell, conception and design, analysis and interpretation of data; drafting the manuscript; revision of manuscript; final approval.

Disclosures
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