Injection Medialization Laryngoplasty in Children

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Objective: To review our experience with vocal fold injection medialization in children.

Design: Retrospective case series.

Setting: Tertiary care academic children’s hospital.

Patients: All pediatric patients at our institution who underwent injection laryngoplasty for vocal fold medialization from 2003 to 2009.

Main Outcome Measures: Age, sex, indication for injection, injection material, surgical and anesthetic technique, outcomes including effect on voice and swallowing, and complications.

Results: Thirteen patients underwent 27 injections. Mean patient age was 8.0 years (range, 1.3-18.0 years). The causes of glottic insufficiency included prolonged intubation (6 patients, 46%), patent ductus arteriosus ligation (2 patients, 15%), other cardiac surgery (2 patients, 15%), neck surgery or trauma (2 patients, 15%), and postviral status (1 patient, 8%). Eight patients had vocal fold paralysis or paresis; 3 had vocal fold atrophy; and 2 had vocal fold scarring. Indications for surgery included hoarseness (11 patients), aspiration (5 patients), and dysphagia without aspiration (1 patient). Materials injected included Gelfoam (n=13), Radiesse Voice (n=10), and Radiesse Voice Gel (n=4). The average number of injections per patient was 2.1 (range, 1-9). Patients experienced improvement in symptoms (subjective or objective) after injection in 24 of 27 cases (89%); 15 of 16 injections in patients with hoarseness led to improvement (94%); and 11 of 13 injections in patients with dysphagia or aspiration led to improvement (85%). One patient experienced 2 days of inspiratory stridor postoperatively, which resolved spontaneously. There were no other complications.

Conclusions: This study supports injection laryngoplasty as a safe and effective intervention for children with glottic insufficiency. Further prospective studies are necessary to confirm these findings.


VOCAL FOLD IMMOBILITY (VFI) is defined as the absence or reduction of motion of the true vocal fold secondary to impairment of the recurrent laryngeal nerve, fixation of the cricoarytenoid joint, or scarring of the vocal fold itself. Vocal fold immobility in children has a broad differential diagnosis and a variety of management strategies depending on age and cause.

Unilateral VFI and bilateral VFI in children are distinct clinical entities that can have different presenting symptoms and causes and require different treatment techniques. The principal concern in bilateral VFI is possible airway obstruction, whereas the primary consequences of unilateral VFI in children are hoarseness and aspiration. Treatment techniques are designed to address these problems. The technique chosen for treatment of VFI depends largely on the cause and the severity of symptoms. In some cases of VFI in the neonate without significant stridor or aspiration, observation alone may be sufficient. Conversely, airway obstruction may occur in very young children with unilateral VFI owing to the small size of the neonatal larynx, potentially necessitating a tracheotomy. The full range of treatments for pediatric unilateral VFI may include observation, speech therapy, injection medialization laryngoplasty, thyroplasty, and surgical reinnervation. In cases of airway obstruction, tracheotomy may be indicated. As airway compromise due to unilateral VFI will improve over time in most cases, permanent lateralization procedures are best deferred for several years.

After a period of caution with regard to the use of injectables following the well-publicized occurrence of late complica-
Reasons for laryngoplasty injection include effect on voice and swallowing, and complications associated with polytetrafluoroethylene (Teflon: DuPont, Wilmington, Delaware), injection laryngoplasty has experienced a renaissance with such materials as gelatin sponge (Gelfoam; Pfizer, New York, New York), acellular dermis (Cymetra; LifeCell Corp, Branchburg, New Jersey), calcium hydroxylapatite (Radiesse Voice; Bioform Medical, San Mateo, California), and sodium carboxymethylcellulose aqueous gel (Radiesse Voice Gel; Bioform Medical). While extensive reviews of outcomes associated with polytetrafluoroethylene have been written about injection laryngoplasty for the problems associated with VFI in children.

The purpose of this study is to describe the clinical experience at a single institution with injection medialization laryngoplasty for VFI in the pediatric population. Attention is specifically given to indications, materials injected, surgical technique, and speech and voice outcomes. Several instructive cases are discussed in detail.

### Methods

This study is a retrospective case series and medical record review encompassing all patients who have undergone injection laryngoplasty for vocal fold medialization from January 2001 through August 2009 at the Children’s Hospital of Pittsburgh of UPMC. The protocol underwent review and approval by the University of Pittsburgh institutional review board in compliance with federal guidelines. Patients were identified by searching our medical record database using current procedural terminology (CPT) codes for direct laryngoscopy with injection or microlaryngoscopy with injection (31570, 31571). Initially, medical records of 91 patients were identified for study. Because the CPT code is the same for all types of laryngeal injection (eg, cidofovir injection for papillomatosis), each record was reviewed in detail, and only patients who underwent injection laryngoplasty for VFI were included. Qualifying medical charts were reviewed thoroughly.

Main outcome measures included patient demographics, indication for injection, material injected, surgical technique, outcomes including effect on voice and swallowing, and complications. Data were compiled from otolaryngology and speech therapy office notes, operative reports, and reports of assessments such as modified barium swallow (MBS), fiberoptic endoscopic evaluation of swallowing (FEES), and salivagram. For each patient, preoperative and postoperative data were compared when available. Duration of effects on voice and swallowing were calculated using patient reports and diagnostic assessments. Subjective improvement in voice and swallowing was determined based on patient and caregiver reports and clinician impression.

### Results

The Table summarizes the causes of VFI, interventions, and outcomes by individual patient. Thirteen patients underwent 27 injections. Mean (SD) patient age was 8.0 (5.4) years (range, 1.3-18.0 years) Eight patients were boys (62%), and 5 patients were girls (39%). The causes of glottic insufficiency included prolonged intubation with prematurity (6 patients, 46%), patent ductus arteriosus ligation (2 patients, 15%), other cardiac surgery (2 patients, 15%), postviral and/or idiopathic cause (1 patient, 8%), neck surgery (1 patient, 8%), and neck trauma (1 patient, 8%). Eight patients had vocal fold paralysis or paresis; 3 had vocal fold atrophy; and 2 had vocal fold scarring. Laterality of lesion was left in 7 cases (54%), right in 3 cases (23%), and bilateral in 3 cases (23%). Treatments used prior to surgery most commonly included antireflux medication (6 cases, 46%), speech therapy (4 cases, 31%), and Nissen fundoplication (3 cases, 23%). Indications for surgery included hoarseness (11 patients, 85%), aspiration (5 patients, 39%), and dysphagia without aspiration (1 patient, 8%).

Anesthetic techniques included spontaneous ventilation in 13 cases (48%), intubation in 10 cases (37%), jet ventilation in 2 cases (7%), and general anesthesia via tracheostomy in 2 cases (7%). The mean (SD) number of injections per patient was 2.1 (2.2) (range, 1-9). Eight patients required only 1 injection; 2 patients had 2 injections; 2 patients had 3 injections; and 1 patient had 9 injections. Materials injected included Gelfoam (n = 13),

### Table. Summary of Demographics, Treatment, and Outcomes by Patient

<table>
<thead>
<tr>
<th>Patient Sex/Age, y</th>
<th>Cause</th>
<th>Injections, No.</th>
<th>Indication</th>
<th>Material(s)</th>
<th>Outcome*</th>
</tr>
</thead>
<tbody>
<tr>
<td>M/11.3</td>
<td>Prolonged intubation</td>
<td>1</td>
<td>H</td>
<td>GF</td>
<td>Lost to follow-up</td>
</tr>
<tr>
<td>M/14.5</td>
<td>Neck trauma (GSW)</td>
<td>1</td>
<td>H</td>
<td>RV</td>
<td>Improved, stable</td>
</tr>
<tr>
<td>F/1.4</td>
<td>Neck surg (ECMO)</td>
<td>1</td>
<td>H, A</td>
<td>GF</td>
<td>Improved, stable</td>
</tr>
<tr>
<td>M/5.5</td>
<td>Post URTI/idopathic</td>
<td>2</td>
<td>H, D</td>
<td>GF, RV</td>
<td>Improved, Rx ongoing</td>
</tr>
<tr>
<td>M/6.3</td>
<td>Prolonged intubation</td>
<td>2</td>
<td>H</td>
<td>GF</td>
<td>Improved, Rx ongoing</td>
</tr>
<tr>
<td>M/6.1</td>
<td>Prolonged intubation</td>
<td>3</td>
<td>H, A</td>
<td>GF, RV</td>
<td>Thyroplasty</td>
</tr>
<tr>
<td>F/16.0</td>
<td>PDA ligation, prolonged intubation</td>
<td>1</td>
<td>H, A</td>
<td>GF</td>
<td>Improved, short follow-up</td>
</tr>
<tr>
<td>M/7.4</td>
<td>Heart surgery, heart transplant</td>
<td>1</td>
<td>H</td>
<td>RV</td>
<td>Improved, short follow-up</td>
</tr>
<tr>
<td>F/2.3</td>
<td>Prolonged intubation</td>
<td>1</td>
<td>A</td>
<td>GF</td>
<td>Improved, stable</td>
</tr>
<tr>
<td>M/2.5</td>
<td>PDA ligation, prolonged intubation</td>
<td>9</td>
<td>A</td>
<td>GF, RV</td>
<td>Improved, Rx ongoing</td>
</tr>
<tr>
<td>F/5.5</td>
<td>Prolonged intubation</td>
<td>3</td>
<td>H</td>
<td>GF, RV</td>
<td>Improved, stable</td>
</tr>
<tr>
<td>M/18.0</td>
<td>Heart surgery (TGV)</td>
<td>1</td>
<td>H</td>
<td>GF</td>
<td>Not improved</td>
</tr>
<tr>
<td>F/7.5</td>
<td>Prolonged intubation</td>
<td>1</td>
<td>H</td>
<td>RV</td>
<td>Improved, short follow-up</td>
</tr>
</tbody>
</table>

*Abbreviations: A, aspiration; D, dysphagia without aspiration; ECMO, extracorporeal membrane oxygenation; GF, Gelfoam (Pfizer, New York, New York [gelatin sponge]); GSW, gunshot wound; H, hoarseness; PDA, patent ductus arteriosus; RV, Radiesse Voice (Bioform Medical, San Mateo, California [calcium hydroxylapatite]); RVG, Radiesse Voice Gel (Bioform [sodium carboxymethylcellulose aqueous gel]); Rx, treatment; TGV, transposition of great vessels; URTI, upper respiratory tract infection.

*Short follow-up indicates shorter than 3 months.

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Radiesse Voice (n=10), and Radiesse Voice Gel (n=4). The Figure demonstrates the typical appearance before and immediately after true vocal fold injection medialization laryngoplasty with Gelfoam.

The injection needle chosen corresponded to the material injected. Gelfoam was injected using a Bruening syringe with a 19-gauge needle. Radiesse Voice and Radiesse Voice Gel were injected using the standard syringe and 25-gauge needle included with the product. The average volume of material injected per case was 0.26 mL for Radiesse Voice and 0.27 mL for Radiesse Voice Gel. The volume of Gelfoam injected was recorded as either number of clicks using a Bruening syringe (average number of clicks, 3.9) (n=7) or volume in mL (average volume, 0.5 mL) (n=5).

For the 3 patients who received multiple injections with Gelfoam, mean (SD) time between injections was 9.7 (3.4) weeks (range, 5.0-15.0 weeks). For the 2 patients who underwent repeated injections with Radiesse Voice, the mean (SD) time between injections was 31.6 (12.3) weeks (range, 6.7-42.2 weeks) No patients in this study had more than 1 injection with Radiesse Voice Gel.

Patients experienced improvement in symptoms (subjective or objective) after injection in 24 of 27 cases (89%); 15 of 16 injections in patients with hoarseness led to improvement (94%); and 11 of 13 injections in patients with dysphagia or aspiration led to improvement (85%). Mean (SD) duration of voice improvement for Gelfoam (n=9) was 6.1 (8.1) weeks (range, 1.7-27.6 weeks), and for Radiesse Voice Gel (n=4), it was 5.6 (4.7) weeks (range, 3.1-12.5 weeks). Mean (SD) duration of swallowing improvement for Radiesse (n=6) was 24.0 (8.6) weeks (range, 11.3-33.9 weeks), and for Gelfoam (n=3), it was 18.0 (14.3) weeks (range, 9.5-34.6 weeks).

Comparable objective evaluations were sporadic, with preoperative and postoperative data available for voice in 2 cases (3 injections) and swallowing in 3 cases (5 injections). In the 5 injections with objective preoperative and postoperative swallowing data, measurable improvement was seen 4 of 5 times (80%).

One patient experienced 2 days of inspiratory stridor after bilateral vocal fold injection, which resolved spontaneously. There were no other complications. Several cases were particularly instructive and are discussed below.

**CASE 1**

A 6-year-old boy born at 25 weeks’ gestation had a history of anterior and posterior graft laryngotracheal reconstruction for subglottic stenosis due to prolonged intubation. Following successful decannulation with a stable airway at age 3 years, the principal airway complaints were hoarseness and breathiness. A scarred and atrophic right true vocal fold was treated with injection laryngoplasty using Gelfoam. The patient experienced a clinically significant improvement in vocal quality that lasted for 4 months and then subsided to baseline. Reinjection was planned with Radiesse Voice but was delayed secondary to an episode of pneumonia requiring several weeks of ventilatory support. Injection was then carried out using Radiesse Voice followed by several weeks of slight improvement and then return to baseline. A third injection using Radiesse Voice was attempted, but there was extrusion of the material and difficulty achieving medialization possibly due to dense scarring within the true vocal fold. There was no improvement in voice postoperatively. The patient subsequently underwent type 1 thyroplasty with an expanded polytetrafluoroethylene implant (GORE-TEX; W. L. Gore & Associates, Newark, Delaware). There was resultant marked stable improvement in voice.

**CASE 2**

A 16-month-old girl sustained right vocal fold paralysis due to extracorporeal membrane oxygenation cannula placement in the right neck 14 months prior to presentation. The patient had a weak cry, and aspiration was demonstrated on MBS. After treatment with speech therapy did not result in significant improvement of as-
piration and hoarseness, right true vocal fold injection medialization laryngoplasty was performed using Gelfoam. One week postoperatively, FEES showed no laryngeal penetration or aspiration. Vocal quality was improved. Speech therapy was continued. One year after injection, FEES revealed a paralyzed paramedian right true vocal fold, good glottic closure, and no evidence of aspiration or penetration.

CASE 3

A 5-year-old boy presented with frequent sighing and a choking sensation while eating that occurred several times per week. The symptoms began several weeks after a severe upper respiratory tract infection. Left true vocal fold immobility was diagnosed on flexible laryngoscopy. Gelfoam injection resulted in cessation of choking events and sighing behavior for 2 months. Rejection with Radiesse Voice Gel resulted in relief of symptoms. At 6-month follow-up, symptoms had not recurred, and flexible laryngoscopy revealed an immobile vocal fold with good compensatory closure.

CASE 4

A 5-year-old girl born at 25 weeks' gestation and requiring 3 months of intubation after birth presented with aphonia. Evaluation revealed bilateral VFI most likely secondary to bilateral arytenoid fixation. Left-side Gelfoam injection resulted in moderate postoperative stridor, which resolved after 2 days. The patient was observed in the hospital overnight and discharged on postoperative day 1. Functional voicing was achieved and lasted 1.5 months. Subsequent bilateral injection with Gelfoam had similar results, with a significant subjective improvement in voice. A third injection into only the left true vocal fold using Radiesse Voice Gel resulted in a durable improvement lasting for at least 7 months, the time of most recent follow-up.

COMMENT

Vocal fold immobility is one of the most common abnormalities of the pediatric larynx. Numerous treatments exist for the management of dysphonia and aspiration secondary to vocal fold immobility, including speech therapy, injection laryngoplasty, thyroplasty, and reinnervation techniques.

Emery and Fearon reviewed 71 cases of vocal fold paralysis and found the most common causes to be trauma to the recurrent laryngeal nerve, central neurologic abnormality, and idiopathic causes. Other contributing causes were birth trauma, anoxia, genetic malformations, and peripheral neuropathy. Tucker reviewed 30 pediatric cases with VFI, and of 8 unilateral cases, 3 were congenital, 3 were due to closed neck injury, and 2 were due to surgical trauma. Unilateral vocal fold paralysis was treated with speech therapy in 8 cases, tracheotomy in 6, reinnervation in 3, absorbable gelatin injection in 2, and surgical medialization in 1. All tracheotomized patients were decannulated within 6 to 18 months. Tucker further found that neither patient injected with absorbable gelatin required further injections once the absorbable gelatin had been absorbed, which suggests that the gradual relateralization allowed for adequate compensatory mechanisms to develop.

Several investigators have sought to characterize the role of injection medialization laryngoplasty for pediatric VFI. Levine et al described 3 children with severe aspiration secondary to VFI who were treated with vocal fold injections using absorbable gelatin sponge or Teflon. The procedure allowed decannulation in all 3 patients, and 1 was able to begin oral feedings. Daya and colleagues reviewed a series of 102 patients presenting with vocal fold paralysis. Only 2 of these patients underwent injection medialization laryngoplasty. Teflon was used in both cases, resulting in improved vocal quality in one patient and granuloma formation requiring surgical removal in the other. Voice outcome data were not available for the second patient.

Patel and colleagues described 4 cases of children with symptomatic unilateral VFI treated with vocal fold injection using Cymetra. Improvement of preoperative symptoms was seen in all 4 cases. Repeat injections were used in 1 case after 3 and 12 months. In the remaining cases, repeated injection was not necessary during the documented follow-up periods, which ranged from 4 to 6 months.

In a study analyzing perceptual voice characteristics in pediatric unilateral VFI, Shah and colleagues compared voice characteristics between patients who eventually underwent surgical intervention and those who did not. They found a statistically significant difference in breathiness between these groups prior to surgery. Seven patients in the intervention group underwent injection medialization laryngoplasty. Postoperative evaluations were not included in the study.

Sipp and colleagues described 12 children who underwent 19 injections for vocal fold medialization. Collagen products seemed to provide beneficial effects for 4 to 6 months, autologous fat for 1 to 6 months, Radiesse Voice for 4 months, and hydrated porcine gelatin powder (Surgifoam; Johnson & Johnson, Somerville, New Jersey) for 4 weeks to 4 months. Kwon and Buckmire nicely summarize various materials available for injection medialization laryngoplasty and their characteristics.

Anticipated duration of effect for a particular injectable material is a characteristic that, though somewhat variable, is of significant interest. Temporary or short-acting materials can give information as to whether the defect is correctable with medialization prior to undertaking more permanent treatment efforts such as laryngeal framework surgery, information that is especially useful in cases where return of laryngeal function is expected, as in neurapraxia. While short-acting agents such as Gelfoam and Radiesse Voice Gel are expected to last only 6 to 8 weeks, several cases in our study had a substantially longer duration of effect, even without interval recovery of vocal fold mobility. In cases 2 and 3, the subjects experienced a durable improvement in symptoms after a single injection with Gelfoam in the absence of visually detectable recovery of vocal fold movement. This effect has been noted by other authors. One explanation of these findings, as previously proposed by Tucker,
is that the gradual resorption of injectable material allows the patient to develop compensatory techniques for reducing the symptoms of glottic insufficiency, especially if speech therapy is used. While speech therapy has been demonstrated to be effective in older children, its role in younger children is less clearly defined, and its success depends on the age and maturity of the child.

One possible alternative explanation for lasting improvement with a short-acting material is that injection may result in fibrosis or scar formation, which increases the bulk of the immobile or atrophied vocal fold.

Comparison among patients in this study was limited by the absence of standardized data collection in many instances, with several physicians using differing terminology to describe the same phenomena and using somewhat different management techniques. The variability in the management of the patients in our series results from a combination of factors, including the heterogeneity of our patient population and varying practice preferences of the pediatric otolaryngologists in our group who treated these patients. These problems are inherent in retrospective reviews. We plan to conduct a prospective study using predetermined algorithms for swallowing evaluation and assessment of voice quality. A multicenter study may be necessary to achieve sample sizes that would allow generalization of findings to the population at large. An ideal protocol would use instrumental swallowing studies such as FEES and MBS preoperatively and at regular intervals postoperatively in addition to consistent use of pediatric voice quality-of-life instruments and objective evaluations of voice.

In conclusion, there are a variety of causes of VFI in children, which can be managed with several treatment techniques. Injection medialization laryngoplasty in children is 1 such technique, and it can lead to improvement in hoarseness, dysphagia, and aspiration. Injection laryngoplasty was a safe and effective intervention in this group of children with glottic insufficiency. Further prospective studies with standardized methods of evaluation are necessary to more completely assess this increasingly accepted technique.

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Analysis and interpretation of data: Cohen and Simons.

Drafting of the manuscript: Cohen and Simons.

Critical revision of the manuscript for important intellectual content: Mehta, Maguire, and Simons.

Study supervision: Mehta, Maguire, and Simons.

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REFERENCES


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