

# Laryngeal Reinnervation for Paralytic Dysphonia in Children Younger Than 10 Years

Marshall E. Smith, MD; Nelson Roy, PhD, CCC-SLP; Dan Houtz, MA, CCC-SLP

**Objective:** To study the effectiveness of ansa-recurrent laryngeal nerve laryngeal reinnervation to improve glottal incompetence causing dysphonia and dysphagia for children with unilateral vocal fold paralysis.

**Design:** We reviewed a series of consecutive cases treated from January 1, 2006, through December 31, 2011.

**Setting:** Otolaryngology division of a children's hospital.

**Patients:** Thirteen children with unilateral vocal fold paralysis.

**Main Outcome Measures:** Surgical complications, parent surrogate quality-of-life measures, global overall assessment of improvement, and auditory perceptual assessment.

**Results:** Thirteen children underwent laryngeal reinnervation. Ages ranged from 2.2 to 8.8 years (mean [SD] age, 5.3 [2.6] years). No major complications were identified. Nine children had preoperative and 6- to 12-month postoperative data on voice and swallowing. Mean

parental global voice rating (0 indicates no voice; 100%, normal voice) changed from 43% (range, 20%-65%) preoperatively to 79% (range, 50%-100%) postoperatively. Regarding perceptual assessment, the mean GRBAS (Grade, Roughness, Breathiness, Asthenia, Strain) Rating Scale sum score (0 indicates normal voice; 15, profoundly abnormal voice) improved from 6.3 to 2.9. Parental assessment of dysphagia with liquids also improved for all children with preoperative symptoms and worsened for none.

**Conclusions:** Our early experience suggests that ansa-recurrent laryngeal nerve laryngeal reinnervation is a safe and effective treatment for unilateral vocal fold paralysis with symptomatic dysphonia and dysphagia in young children. The procedure has advantages compared with other treatments. This option should be discussed with parents when the paralysis is identified. The child should be observed for several years in the event that voice and swallowing symptoms from glottal incompetence do not improve.

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**U**NILATERAL VOCAL FOLD paralysis (UVFP) in infants and young children is a condition commonly encountered by the pediatric otolaryngologist, especially in pediatric tertiary hospitals with a cardiac surgery program. These procedures, and other pediatric neck or chest surgical procedures that intersect with the course of the vagus or the recurrent laryngeal nerves, can cause vocal fold paralysis. The symptoms of dysphagia, dysphonia, and stridor may result.

In the short term, these problems may prolong hospitalization, resulting in aspiration, pneumonia, and the need for an alternative feeding route. In the long term, difficulty with oral feeding, need for diet modifications, and delays in speech and oral communication occur.

Our institution has a well-established program in congenital heart disease and large neonatal intensive care units. Some children unfortunately develop UVFP as a complication of treatment. An example of the initial treatment is patent ductus arteriosus ligation. A prospective study from our center of a large group of infants who underwent patent ductus arteriosus ligation found that infants weighing less than 1250 g at the time of the procedure had a 24% risk of UVFP.<sup>1</sup> This increased risk in smaller infants has also been well documented at other centers.<sup>2,3</sup> Any cardiac procedure that includes dissection at or near the aortic arch puts the left recurrent laryngeal nerve (RLN) at risk.

In observing these children, we have found that vocal fold mobility infrequently recovers. Despite this reduced mobility, patients often progress to safe swal-

**Author Affiliations:** Division of Otolaryngology-Head and Neck Surgery, Primary Children's Medical Center, University of Utah School of Medicine (Dr Smith), Department of Communication Sciences and Disorders (Dr Roy), and University Hospital (Mr Houtz), University of Utah, Salt Lake City.

lowing without a supplementary feeding route. Usually feeding and airway are of primary concern in young infants, and voice and speech are not a focus of attention for the parents or the pediatrician. Some of these children do not recover completely and continue to experience voice and swallowing problems. Regarding voice production, the child may be unable to produce an audible voice of sufficient volume for typical communication. They cannot be heard from another room in the home or may run out of air when speaking. These children are often born prematurely and have developmental delays that affect speech. The voice problem compounds these delays. Regarding swallowing, although most children with UVFP eventually compensate and are able to swallow, their diet may require modification to swallow safely. They may continue to choke or cough with thin liquids. Although they do not aspirate sufficiently to develop pneumonia, chronic intermittent microaspiration may cause or perpetuate chronic reactive airway disease.

The treatment of UVFP in infants and young children is controversial. In our view, the controversy is due to the co-occurrence of several factors that include the following: (1) an inadequate understanding of the natural history of UVFP in infants and young children regarding functional long-term effects on voice and swallowing, (2) poorly defined indications for surgical intervention, and (3) a variety of treatment options without well-documented treatment outcomes.

Treatment options in use for UVFP include injection laryngoplasty, medialization laryngoplasty (also called type I thyroplasty), and reinnervation. These treatments have all been reported in case reports or small case series to be used in children with UVFP.<sup>4-8</sup> Regarding injection laryngoplasty, the injection implants in the United States include micronized acellular dermal matrix (Cymetra; LifeCell Corporation), hyaluronic acid gels, carboxymethylcellulose gel (Radiesse Voice Gel; Merz Aesthetics, Inc),<sup>9</sup> and calcium hydroxylapatite microspheres in gel suspension (Radiesse Voice; Merz Aesthetics, Inc). Although the calcium hydroxylapatite microspheres are approved for use in adults, they undergo eventual partial resorption, and the mean duration of clinical effect is reported to be 18.6 months.<sup>10</sup> These implants also have unfavorable viscoelastic properties for phonation if inadvertently placed in the lamina propria.<sup>11</sup> Children do not have a well-defined vocal ligament, so the potential for medial migration of the implant is high. For these reasons, we believe that the calcium hydroxylapatite microspheres should not be used in children. The other injectable therapies are well tolerated, but temporary. They provide short-term improvement in symptoms while waiting to see whether vocal fold tone or movement will recover sufficiently to improve symptoms. Several recent reports suggest a benefit of early injection of these materials because the treatment may reduce the need for thyroplasty.<sup>12,13</sup> This approach has not been studied in children. Medialization thyroplasty has been reported in several small case series, with a total of only 23 children.<sup>14-16</sup> Although the procedure is intended to be permanent, in our view, it is not a reasonable option for young children. The soft laryngeal cartilage does not hold a polymeric silicone (Silastic; Dow Corning) or a polytet (Gor-

tex; WL Gore & Associates) implant well, and the long-term fate of these foreign-body implants on the larynx is unknown. The procedure cannot be performed using local anesthesia to adjust the implant and optimize the voice. This procedure has been used in children with general anesthesia and fiberoptic laryngoscopy, although this method is less precise. As the larynx grows, the implant is likely to shift position. The implant becomes surrounded by a fibrous capsule that makes the procedure difficult to revise.

The laryngeal reinnervation treatment option remains to be reviewed.<sup>17</sup> The following 2 variations of this approach to UVFP have been investigated: ansa hypoglossi-to-RLN anastomosis,<sup>18</sup> and nerve-muscle pedicle implantation to the adductor laryngeal muscles.<sup>19</sup> Laryngeal reinnervation has potential for life-long improvement in glottal incompetence for infants and young children. No foreign implant material is used, and no encroachment on the airway occurs owing to an injection or a medialization. The procedure is technically less demanding than thyroplasty, because no need for intraoperative judgment is required in placing a prosthetic implant. The procedure would be expected to have life-long effects. Infants and young children have a high capacity to regenerate neural conduction after peripheral nerve injuries. Large-case series of adults who underwent ansa-RLN laryngeal reinnervation are available documenting its efficacy.<sup>20</sup> Small-case series of ansa-RLN reinnervation have been reported recently in children as young as 3 years.<sup>8,21</sup> We studied 6 adolescents and young adults with UVFP who underwent ansa-RLN laryngeal reinnervation.<sup>22</sup> We found improvements in voice averaging up to 82% of normal, based on patient self-assessment and blinded listener ratings. On the basis of this experience, we believed that offering the procedure to younger children who have glottal incompetence from UVFP is reasonable.

## METHODS

We reviewed a series of consecutive cases of children younger than 10 years with UVFP and symptomatic glottal incompetence treated with ansa-RLN laryngeal reinnervation at our institution since 2006. Approval from the institutional review board was obtained. We reviewed medical records for documentation of outcomes. Outcome measures reviewed included surgical complications, parent surrogate quality-of-life measures, global overall assessment of improvement, and auditory perceptual assessment. The surrogate voice-related quality-of-life instrument used was the pediatric Voice Handicap Index (pVHI).<sup>23</sup> Parents also reported a global 0% to 100% assessment of voice, analogous to a rating scale used for spasmodic dysphonia,<sup>24</sup> where 0% indicates no voice and 100%, a normal voice. Auditory perceptual rating of voice was performed by the surgeon at the time of clinic visit following the GRBAS (Grade, Roughness, Breathiness, Asthenia, Strain) Rating Scale.<sup>25</sup> In this scale, each variable is given a score from 0 to 3 (0 indicates normal; 3, severely abnormal). The sum of the rating for each variable was tallied (0 indicates lowest; 15, highest). Swallowing function was assessed by parent report regarding difficulty swallowing thin liquids. The following responses were assigned on a 5-point scale where 1 indicates never; 2, almost never; 3, sometimes; 4, almost always; and 5,

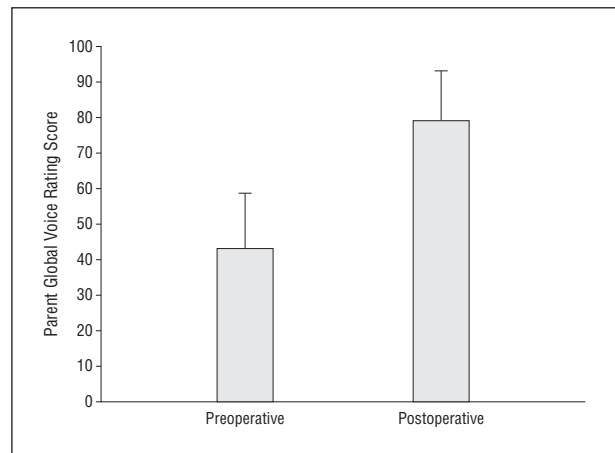
always. Pretreatment-posttreatment comparisons used the Wilcoxon signed rank nondirectional test for matched pairs.

## RESULTS

Thirteen children (9 boys; mean [SD] age, 5.3 [2.6] years) underwent the ansa-RLN laryngeal reinnervation procedure from January 1, 2006, through December 31, 2011. Their ages ranged from 2.2 to 8.8 years. Five patients were 2 years of age; 1, 3 years; 3, 6 years; 1, 7 years; and 3, 8 years. Twelve patients underwent patent ductus arteriosus ligation in infancy and 1 underwent coarctation of the aorta repair. No early postoperative complications were identified. One patient developed a hypertrophic surgical scar. Two patients did not have adequate documentation of their voice and swallowing outcomes with the ratings described in the "Methods" section and were excluded from the analysis. Eleven had preoperative voice data ;9 had preoperative and 6- to 12-month postoperative voice data. **Figure 1** shows the mean parental global voice rating improved from 43% (range, 20%-65%) to 79% (range, 50%-100%). This difference was statistically significant (difference, 36;  $P=.01$ ). Except for an 8-year-old patient who had a score of 50%; all others had a postoperative score of 70% or higher. Of these, 6 scores were 80% or higher, and 2 scores ranged from 90% to 100% (**Figure 2**). Regarding perceptual assessment with GRBAS sum score for the 9 patients with preoperative and postoperative data, **Figure 3** shows the individual patient data. The average GRBAS sum score improved from 6.3 to 2.9 ( $W, 45; P<.01$ ). Preoperative pVHI scores on 4 subjects ranged from 17 to 66 (mean, 40.5). The mean postoperative pVHI score was 22.5 ( $W, 6$ ; differences were not significant). Three additional patients had postoperative pVHI scores with an overall mean for the 7 patients of 22.6 (range, 6-36). For 9 patients, preoperative and postoperative parental assessment of dysphagia with liquids was assessed. The individual patient results are shown in **Figure 4**. The average preoperative dysphagia score was 3.7, and postoperative score was 1.6 ( $W, 21; P=.05$ ). Four patients had 6- and 12-month postoperative ratings; we detected no statistical difference between parental or GRBAS ratings at these intervals.

## COMMENT

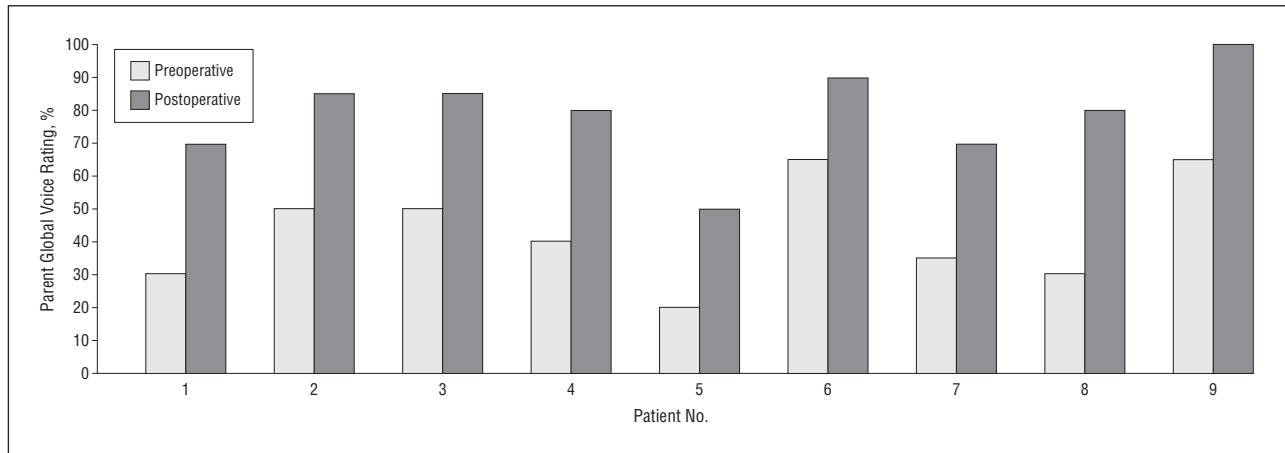
This retrospective review of our early experience with young children who undergo ansa-RLN laryngeal reinnervation for UVFP suggests a positive clinical effect in improving voice and swallowing, as assessed by parent report and perceptual assessment. Our findings also suggest that 6 months constitute sufficient time for reinnervation to show positive improvement, with stable results at 12 months. This finding is consistent with those reported by others.<sup>20</sup> The procedure can be performed safely without significant risk of complications relating to airway or wound infection. This low risk was reported in a recent review of adult patients that compared complication rates of reinnervation and thyro-



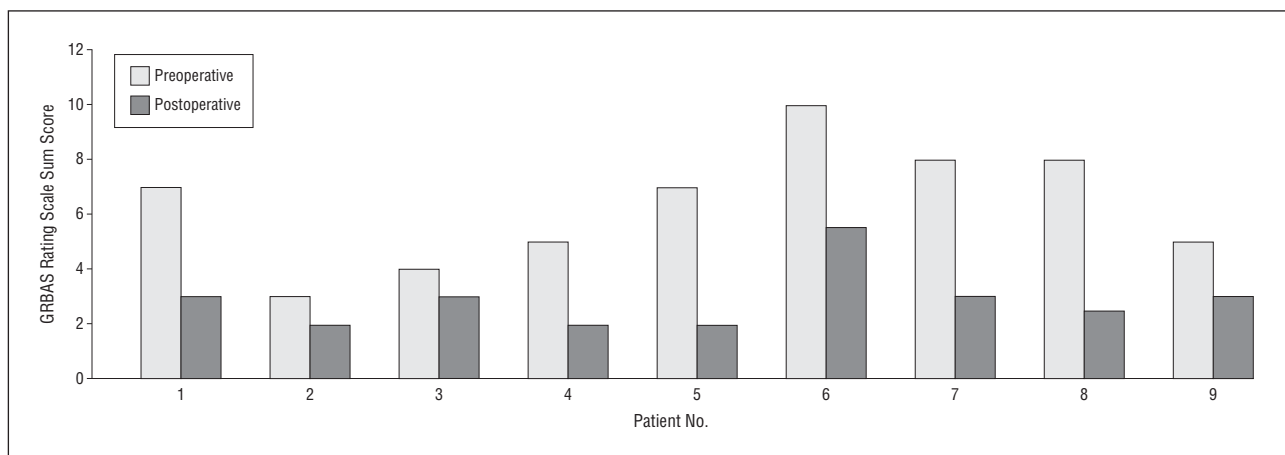
**Figure 1.** Mean parent global rating of voice in the 9 patients undergoing laryngeal reinnervation with preoperative and 6- to 12-month postoperative voice and swallowing data available. Whiskers represent standard deviations.

plasty.<sup>26</sup> Many children with UVFP have a history of cardiac disease. Consultation with the pediatric cardiologist is helpful in assessing the operative risk for these patients.

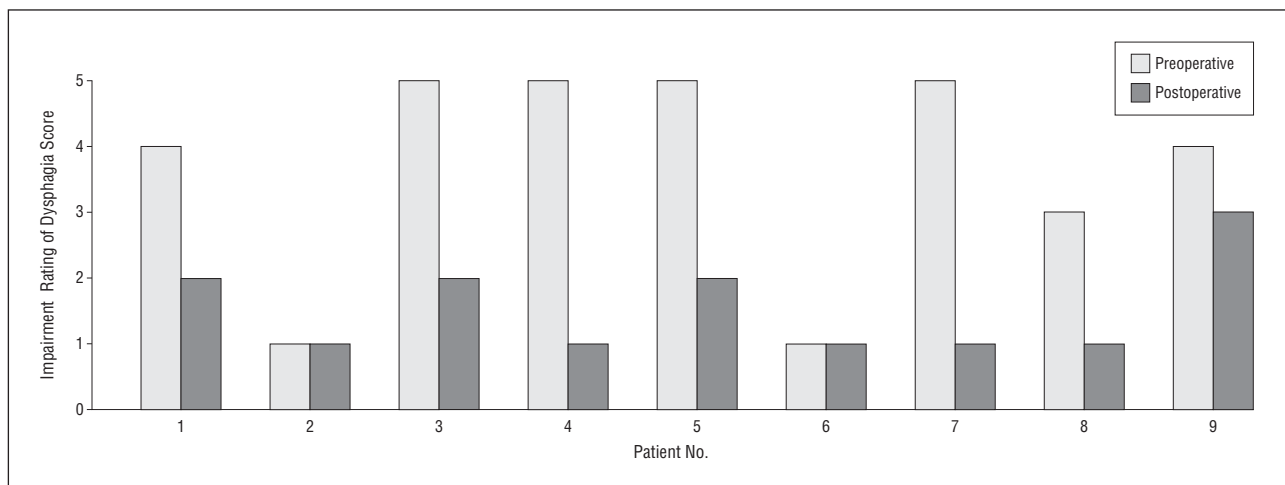
The study has limitations inherent in a retrospective review, with some missing data points. The study also uses outcome measures that involve subjective ratings by the parent and the examiner. The GRBAS Rating Scale is a well-known perceptual rating scale for voice quality measures. The outcome measures regarding voice and swallowing involved parent surrogate ratings. The parent surrogate ratings are necessary for several reasons. Parent surrogate rating of pediatric health, such as the Pediatric Quality of Life Inventory, version 4.0, is a commonly used research tool.<sup>27</sup> We used the pVHI, which has some limitations. The pVHI questions were adapted from the adult VHI, but were not originally designed specifically for children or for children of different age groups, as were the Pediatric Quality of Life Inventory questions. We found this to be the case; the questions did not consistently reflect well the issues involved in vocal impairment for young children. Although our numbers were small, the pVHI did not appear very sensitive to pretreatment-posttreatment changes. A pediatric voice quality-of-life survey instrument is being developed and validated for different age groups that should provide a more robust tool for pediatric voice studies in the future.<sup>28</sup> For our purposes, a global rating of voice impairment from the parent seemed to be more responsive. This change was also reflected in their posttreatment comments, such as "I can hear my child easily from another room now" and "His voice is not quite as loud as his brothers, but is much better." In our study of older children with vocal fold paralysis wherein blinded listener ratings and patient assessment of voice were studied, the results were similar.<sup>22</sup> The mean perceptual visual analog scale rating of dysphonia severity (0 mm indicates a profoundly abnormal voice; 100 mm, a completely normal voice) improved from 50 mm preoperatively to 82 mm postoperatively. Global self-ratings of voice function (0-100%) increased from 31.2% to 81.6% of normal. This improvement indicated that the listener ratings and the patient



**Figure 2.** Individual parent global rating of voice in the 9 patients undergoing laryngeal reinnervation with preoperative and 6- to 12-month postoperative voice and swallowing data available. Ratings ranged from 0 (no voice) to 100% (normal voice).



**Figure 3.** Individual GRBAS (Grade, Roughness, Breathiness, Asthenia, Strain) Rating Scale sum score in the 9 patients undergoing laryngeal reinnervation with preoperative and 6- to 12-month postoperative voice and swallowing data available. Scores ranged from 0 to 3 for each variable, with a highest possible score of 15.



**Figure 4.** Individual parent impairment rating of dysphagia with liquids in the 9 patients undergoing laryngeal reinnervation with preoperative and 6- to 12-month postoperative voice and swallowing data available. Swallowing function was assessed by parent report regarding difficulty swallowing thin liquids, with responses on a 5-point scale where 1 indicates never; 2, almost never; 3, sometimes; 4, almost always; and 5, always.

ratings trended in the same direction with the same magnitude of change. The present study could be strengthened by a similar comparison of listener ratings and parent surrogate ratings.

We also used a parent rating of swallowing impairment with thin liquids, which is more problematic in patients with UVFP. This rating also appeared responsive to pretreatment-posttreatment changes. Swallowing prob-

lems are often intermittent, so that penetration or aspiration may not be always identified on a fluoroscopic or endoscopic swallow study. A more in-depth analysis by use of videofluoroscopic or endoscopic swallowing measures for assessment of oropharyngeal swallow function before and after surgery would augment these subjective observations. These measures would afford improved understanding of changes in swallowing physiology (including the presence or absence and the degree of laryngeal penetration and aspiration) after laryngeal reinnervation.

Voice recordings of children present a significant challenge. Research studies in voice usually require standardized recording conditions, specifically regarding microphone-to-mouth distance to reduce background noise and control intensity. Maintenance of constant microphone position, reading of standardized passages, and repetition of sustained vowel or maximum phonation time is impossible for young children and for some older children. Coaxing or persuading young children to speak in the clinic examination room setting to hear their voice can be difficult. Voice recordings of good quality would be ideal, to allow for perceptual ratings by blinded listeners, as we have in adolescent and adult studies.<sup>22</sup> Although voice recordings were possible with some patients, not enough were available of consistent quality preoperatively and postoperatively to permit evaluation by blinded listeners. This limitation may be overcome with more resources and time and is a goal of our future efforts. Although these results are promising, they should be viewed as preliminary and awaiting verification. Future research is necessary using a larger sample of patients and multiple outcomes measures (subjective and objective), such as blinded listener judgments and acoustic analysis of preoperative and postoperative voice samples.

Our preliminary results indicate that the ansa-RLN laryngeal reinnervation has potential to improve the voice of the child with UVFP significantly. This outcome was also found in a recently published prospective, randomized, multicenter surgical trial of reinnervation vs medialization in adults with UVFP.<sup>29</sup> Patients younger than 52 years had better voices with reinnervation, and older patients had better results with medialization. The only subjects whose GRBAS scores were rated as normal voice quality were in the reinnervation group. This finding suggests that children should also be good candidates for reinnervation, and the potential to improve voice quality is high. Our experience with older children found an improvement in loudness and pitch range, not just voice quality.<sup>22</sup> We expect that younger children will have similar outcomes, although acoustic analysis will be needed to confirm this.

When vocal fold paralysis is identified in these infants, we have found that we must discuss with parents the need to observe these children for several years for voice and swallowing. The initial focus is on feeding, but as the child grows, speech and voice will become more important issues. The otolaryngologist should explain to the parents and the primary care provider early in their evaluation and care that options are available for treating the paralyzed vocal fold when the child is older in

the event it does not recover. Vocal fold paralysis should be kept on the child's problem list. The patients will then be more likely to return for care. Otherwise, the child's voice problem can be neglected by the family, who become used to their child's soft voice and do not recognize it as a problem or as related to the paralyzed vocal fold found several years earlier. The primary care provider may not ask about the voice or ever hear the child speak during his/or her examination.

We do not know the age limit or the time window for reinnervation. These variables likely depend on the degree of nerve injury and the residual population of motor units available for reinnervation, which could vary widely. Denervation atrophy could occur as the child is older, which prevents successful reinnervation. In our view, it is reasonable to intervene as early as it is determined that UFVP will not recover on its own. Conventional practice suggests that at least 1 year is needed; however, we do not have electromyogram-validated prospective studies to confirm this in infants with UVFP. The otolaryngologist must determine that the child's symptoms are sufficient to demonstrate moderate to severe dysphonia and possibly dysphagia with liquids. The operation needs to be safe and technically feasible to conduct the nerve dissection and anastomosis. The age of 2 years seems to qualify as the minimum that meets these criteria, although a younger age may be possible.

In summary, our early experience suggests that ansa-RLN laryngeal reinnervation is a safe and reasonably effective treatment for UVFP with symptomatic dysphonia and dysphagia in young children. Reinnervation has advantages compared with other treatments. This treatment option should be discussed with parents when the paralysis is identified, so the parents understand that this option is available if needed after a period of observation. Children with UVFP should be observed for several years in the event that voice and swallowing symptoms from glottal incompetence do not improve.

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**Correspondence:** Marshall E. Smith, MD, Division of Otolaryngology–Head and Neck Surgery, University of Utah School of Medicine, 50 N Medical Dr, Salt Lake City, UT 84132 (marshall.smith@hsc.utah.edu).

**Author Contributions:** Drs Smith and Roy had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. *Study concept and design:* Smith. *Acquisition of data:* Smith and Houtz. *Analysis and interpretation of data:* Smith, Roy, and Houtz. *Drafting of the manuscript:* Smith and Roy. *Critical revision of the manuscript for important intellectual content:* Smith, Roy, and Houtz. *Statistical analysis:* Smith and Roy. *Administrative, technical, and material support:* Houtz.

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