Systematic review of laryngeal reinnervation techniques

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LITERATURE REVIEW

Systematic review of laryngeal reinnervation techniques

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ABSTRACT

OBJECTIVE: To systematically review outcomes of reinnervation techniques for the management of unilateral vocal fold paralysis (UVFP).

DATA SOURCES: Medline and Cochrane databases for English-language studies published between 1966 and 2009 on the surgical management of UVFP.

REVIEW METHODS: Studies were excluded if they reported on bilateral vocal fold paralysis, used nonhuman subjects, or did not assess clinical outcomes. Outcomes of interest were visual analysis, acoustic analysis, perceptual analysis, and electromyography.

RESULTS: Of 686 initial studies, 14 studies encompassing 329 patients were eligible for analysis. All studies had a case-series design. Of reported patients, 60.2 percent were men, with mean age of 51 years (range, 12-79 years). The most common reinnervation technique was ansa cervicalis-to-recurrent laryngeal nerve (RLN), which was most commonly performed after thyroidectomy (43.5%). Other techniques with reportable outcomes included primary RLN anastomosis, ansa-to-RLN combined with cricothyroid muscle-nerve-muscle pedicle, ansa-to-thyroarytenoid neural implantation, ansa-to-thyroarytenoid neuromuscular pedicle, and hypoglossal-to-RLN. Median postsurgical follow-up was 12 months, and mean time to first signs of reinnervation was 4.5 months (SD 2.9 months). Visual analysis of glottic gap showed the greatest mean improvement with ansa-to-RLN, from 2.25 (SD 0.886) to 0.75 (SD 0.886) mm ($P < 0.01$). Acoustic analysis showed greatest improvement with neural implantation, with a change in mean phonation time from seven (SD 1.22) to 16 (SD 5.52) seconds ($P < 0.01$). Perceptual analysis and electromyography demonstrated improvement in all studies.

CONCLUSION: Reinnervation is effective in the management of UVFP, although the specific method may be dictated by anatomical limitations. Prospective studies utilizing uniform and consistent outcome parameters are necessary.

Unilateral vocal fold paralysis (UVFP) is a common problem in patients who present to the otolaryngologist and has a significant impact on a person's quality of life.[1] The most frequent cause of UVFP is injury to the recurrent laryngeal nerve (RLN).[2] The most common etiologies of RLN injury include extralaryngeal malignancy, trauma, iatrogenic causes, and idiopathic cases.[1] RLN palsy is the most common serious complication of thyroid surgery, ranking among the leading reasons for litigation of surgeons.[3] Even with the use of physiologic nerve monitoring, temporary and permanent RLN palsy still occur at rates of six percent and one percent, respectively.[4] In the United States between 1980 and 1997, the incidence of thyroid cancer increased by 2.4 percent per year; since then, this rate has increased to 6.4 percent per year.[5] Cases of locally advanced thyroid cancer may directly compromise the RLN or lead to intraoperative sacrifice rather than iatrogenic transection.[4] Regardless of the cause of nerve injury, optimal management of UVFP in the face of these increasing trends in surgical thyroid disease is becoming an increasingly relevant issue.

The physical manifestations of UVFP include a forward-tilted arytenoid, loss of movement, and loss of muscle tone, leading to bowing of the vocal fold. The resulting incomplete glottic closure can manifest as dysphonia and aspiration.[6] In addition, laryngeal synkinesis may result from aberrant abductor or adductor reinnervation after RLN damage or repair.[7-9] Current treatment options for UVFP include injection laryngoplasty, medialization thyroplasty, arytenoid adduction, and laryngeal reinnervation techniques. Notable reinnervation strategies include primary RLN anastomosis (primary RLN), ansa cervicalis-to-RLN neurorrhaphy (ansa-RLN), ansa cervicalis-to-thyroarytenoid neural implantation (implantation), ansa cervicalis-to-thyroarytenoid neuromuscular pedicle (NMP), hypoglossal-to-RLN neurorrhaphy (hypoglossal-RLN), and cricothyroid muscle-nerve-muscle neurotization (CT MNM).[10] Injection laryngoplasty with temporary agents such as micronized AlloDerm or gelfoam may supplement reinnervation to provide relief until the anticipated benefits take effect.[11,12]

Compared with the other treatment options, laryngeal reinnervation holds several advantages. Thyroarytenoid muscle tone and bulk loss, which can mitigate the long-term effects of laryngoplasty with changes in the vocal fold

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position as time passes, are avoided.[13] In addition, the preservation of laryngeal anatomy allows for future laryngoplasty procedures should the need arise. Moreover, improvements in voice quality, particularly pitch control, can be achieved without alterations in vocal fold pliability or mucosal wave.[14] Distinct advantages of reinnervation exist in the pediatric population.[15] The procedure is performed under general anesthesia, which allows the surgeon to avoid the fine adjustments needed for medialization laryngoplasty under local anesthesia. The preservation of laryngeal anatomy allows for unaltered development and growth as the child matures.

In light of the increasing rates of certain surgical procedures, the greatest utility in reinnervation lies in the ability to immediately repair an injured, sacrificed, or invaded nerve if identified intraoperatively. Although the authors of several studies have demonstrated the success of reinnervation in animal studies,[16-18] these findings may not correlate with surgical results in human patients.[19] A number of clinical studies in which the authors examined outcomes of individual reinnervation techniques in human subjects have been performed. Although a number of narrative review articles[2,10,20,21] have described these modalities, to date, consistent recommendations are lacking and reports on the different techniques vary. The aim of our study was to systematically review these published reports to ascertain the relative effectiveness and indications of the various techniques, particularly within the intraoperative setting.

Methods

Literature Search

We searched the Medline and Cochrane databases with the following Medical Subject Heading (MeSH) terms filtered for English language and human studies: "recurrent laryngeal nerve" (subheading "surgery") and "unilateral vocal fold paralysis" (subheading "surgery"). This search corresponded to the following word combinations: "Recurrent Laryngeal Nerve/surgery"[MAJR] AND ("humans"[MeSH Terms] AND English[lang]) OR "Vocal Cord Paralysis/surgery"[MeSH Terms] AND ("humans"[MeSH Terms] AND English[lang]). We considered all studies published between January 1966 and December 2009. Reference lists of identified articles were screened for additional relevant studies.

Selection of Cases

Two independent reviewers (B.B.A. and E.M.) assessed each study based on the following exclusion criteria: description of only alternative techniques rather than reinnervation; posterior cricoarytenoid reinnervation for bilateral vocal fold paralysis; review articles; duplicate patients; absence of preoperative values; and exclusive focus on a single age group.

Quality Checks

Quality assessment of each study consisted of four questions pertaining to clinical case series with corresponding values. The purposes of data collection were examined (patient care, 1; research purposes, 2; or not stated, 1). Were the samples consecutive (yes, 2; no, 1; or not stated, 1)? Was the follow-up period of at least one year (yes, 2; no, 1; or not stated, 1)? The final quality check question is whether or not lack of postoperative data or follow up is accounted for (yes, 2; no, 1; or not stated, 1). The results of these checks were quantified into an overall quality score for each study.

Extraction and Analysis of Data

The following data were extracted from each study by two independent reviewers (B.B.A. and E.M.): design, level of evidence, intervention (primary RLN, ansa-RLN, neuromuscular pedicle, implantation, ansa-RLN combined with CT MNM, and hypoglossal-RLN), supplemental interventions (medialization thyroplasty or injection laryngoplasty), outcome measure and parameters (visual, acoustic, subjective perceptual, or electromyography [EMG]), duration of paralysis before reinnervation, duration of follow-up, time until first signs of reinnervation, patient age range, gender, and etiology of UVFP. Novel techniques, including endoscopic approaches, were not included because of the small number of subjects. Patients with no postoperative data because of apparent treatment failure were included. Studies in which patients underwent intraoperative primary RLN repair were included as well, given immediate postoperative measurements were provided. This inclusion was made by the delayed effect of muscle reinnervation.[22]

Data from each of the four outcome measures (visual, acoustic, subjective perceptual, and EMG) from each study were recorded, including mean values, standard deviations, confidence intervals, and/or *P* values when available. The specific scales and units used by each study, along with generalized scales across studies, are described in the results section. Because of ambiguities in methodology and follow-up data, no attempt was made to perform formal meta-analysis.

Results

Study Selection

Of the 686 articles retrieved, 666 articles were excluded because of the inclusion of nonhuman subjects, a description of only alternative techniques rather than reinnervation (such as thyroplasty, laryngoplasty, etc.), reinnervation of posterior cricoarytenoid for bilateral vocal fold paralysis, being review articles, and/or lack of a description of clinical management. After a review of the remaining 20 articles, 10 additional reports were excluded because of duplicate patients,[22-28] a lack of preoperative values,[29] exclusive focus

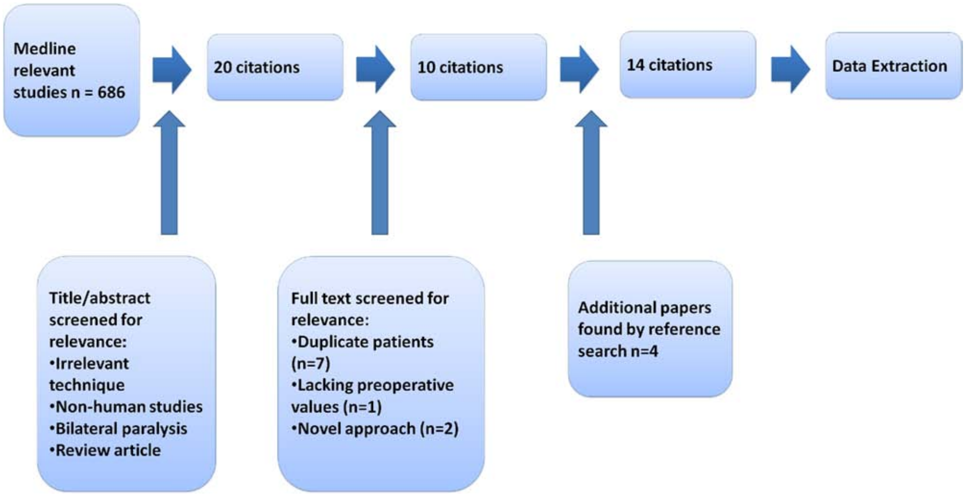

Figure 1 Study selection.

on two children,[15] and focus on a novel approach used on only two patients.[30] From the 284 references of the 10 remaining articles,[31-40] an additional four publications[13,41-43] were identified and included after a manual crosscheck of the bibliography. Unpublished reports were not considered (Fig 1).

Methodological Quality

All included studies were case series with varying levels of quality (Table 1). Eight studies collected some or all data for research purposes. Only three studies used consecutive samples.[35,38,39] All but five[13,31,36,40,43] had a median follow-up period of at least 12 months.

Study Population Characteristics

A total of 329 patients (39.8% male) with a mean age of 51 years (range, 12-79 years) underwent reinnervation procedures. Median presurgical observation time was 15 months (range, 4-108 months). Median postsurgical follow-up was 10 (SD 3.84) months. Median for first signs of reinnervation was four months (SD 2.87 months). Because of a lack of distinction within studies, patient characteristics comprise all 329 surgical subjects, whereas 154 patients had reported preoperative and postoperative data (Table 1). It is also important to note that Miyauchi et al[32] and Maronian et al[42] reported on two

Table 1
Study characteristics

Study	Score	Intervention(s)	Supplemental procedure	Surgical subjects
Miyauchi, 2009[32]	7/8	Primary RLN; Ansa-RLN	None	88
Smith, 2008[35]	7/8	Ansa-RLN	Medialization; injection	6
Lorenz, 2008[38]	7/8	Ansa-RLN ± CT MNM	Injection	46
Su, 2007[37]	7/8	Implantation	None	10
Lee, 2007[39]	7/8	Ansa-RLN ± CT MNM	Injection	25
Chou, 2003[31]	6/8	Primary RLN	None	8
Maronian, 2003[42]	7/8	Ansa-RLN; NMP	Injection	9
El-Kashlan, 2001[36]	5/8	Ansa-RLN + CT MNM	Medialization; injection	3
Paniello, 2000[40]	6/8	Hypoglossal-RLN	None	9
Olson, 1998[33]	6/8	Ansa-RLN	Injection	12
Zheng, 1996[34]	7/8	Ansa-RLN	None	8
Crumley, 1991[13]	4/8	Ansa-RLN	Injection	12
Tucker, 1989[41]	6/8	NMP	None	73
May, 1986[43]	5/8	NMP	Injection	20
Total				154

Primary RLN, primary recurrent laryngeal nerve anastomosis; *Ansa-RLN*, ansa cervicalis to recurrent laryngeal nerve anastomosis; *Medialization*, arytenoid medialization; *Injection*, injection laryngoplasty with micronized AlloDerm or gelfoam; *CT MNM*, cricothyroid muscle-nerve-muscle neuromuscular pedicle; *Implantation*, ansa cervicalis to thyroarytenoid neural implantation; *NMP*, ansa cervicalis to thyroarytenoid neuromuscular pedicle; *Hypoglossal-RLN*, hypoglossal to recurrent laryngeal nerve anastomosis.

Table 2
Etiologies of unilateral vocal fold paralysis for patients undergoing various reinnervation techniques

Etiology	Patients	Ansa-RLN ± CT MNM	Ansa-RLN	Primary RLN	NMP	Implantation	Hypoglossal-RLN
Thyroid cancer ± surgery	117	14	80	12	7	4	
Idiopathic	43	19	15		7	1	2
Mediastinal mass surgery	21	12	1		4	1	3
Spine surgery	16	9	4		1	3	1
Vagal paraganglioma	16	12	3		1		
Aortic surgery	11	7	4				
Skull base tumor	8	1	2		5		
Neck/laryngeal trauma	8	1	3		4		
Parathyroidectomy	7	2		3		1	1
Jugular paraganglioma	3	2	1				
Neck mass excision	3	2					1
Mediastinoscopy	2	1	1				
Esophagectomy	2	2					
PDA ligation	2		2				
Vagal neurofibroma	2	2					
Endarterectomy	2				2		
Scar tissue lysis	2	2					
Chemo/RT for lung cancer	1	1					
Vagal schwannoma	1		1				
Intubation	1		1				
CVA	1						1

Ansa-RLN, ansa cervicalis to recurrent laryngeal nerve anastomosis; *CT MNM*, cricothyroid muscle-nerve-muscle neuromuscular pedicle; *Primary RLN*, primary recurrent laryngeal nerve anastomosis; *NMP*, ansa cervicalis to thyroarytenoid neuromuscular pedicle; *Implantation*, ansa cervicalis to thyroarytenoid neural implantation; *Hypoglossal-RLN*, hypoglossal to recurrent laryngeal nerve anastomosis; *PDA*, patent ductus arteriosus; *Chemo/RT*, chemotherapy and radiotherapy; *CVA*, cerebrovascular accident.

procedures with pooled demographics. Three studies explored cricothyroid reinnervation in patients with high vagal injuries.[36,38,39] Lorenz et al[38] and Lee et al[39] pooled etiologies for patients who underwent ansa-RLN alone versus ansa-RLN combined with CT MNM. Use of supplemental procedures, including thyroplasty and injection laryngoplasty, is noted when available. Etiologies for UVFP were reported for 269 patients (Table 2), with the most common causes being thyroidectomy (43.5%) and idiopathic (16%). One study[41] failed to identify etiologies.

Acoustic Analysis

Acoustic analysis was provided as mean phonation time in seconds (MPT), whereas shimmer and jitter were reported as percentages. Preoperative data from Miyauchi et al[22] were pooled for the two techniques, but postoperative data were distinguishable.

Five studies[31,32,35,37,40] included MPT values (Table 3), all of which demonstrated improvement. Two studies[31,37] supplied *P* values that were statistically significant. Miyauchi et al[22] expressed MPT as a phonation efficiency index, calculated as the ratio of MPT/vital capacity in an attempt to correct for gender differences. Jitter and shimmer were measured in four studies[34,36,37,40] (Table 4), all showing improvement. Each study involved a different technique. Both studies supplying *P* values showed statistical significance.

Visual Analysis

The results of visual analysis were reported as qualitative findings, including change in vocal cord vertical height, vocal cord edge, supraglottic effort, mucosal wave, glottic closure/gap/chink, atrophy/vocalis muscle bulk, vocal fold position, arytenoid movement, and arytenoid position (Tables 5-7). Visual analysis values for Lorenz et al[38] were calculated by the use of logistic regression models; preoperative values were reported as "baseline probability of abnormality" and postoperative values as odds ratios. Maronian et al[42] did not distinguish between the ansa-RLN versus NMP when reporting on visual findings.

Glottic gap was the most commonly reported parameter. A scale of 0 to 3 was used, with 0 corresponding to complete closure and 3 representing fully incomplete. All six studies[31,34,37-39,42] demonstrated improvement, with Lorenz et al[38] and Chou et al[31] including *P* values. Two studies[38,39] recorded an insignificant difference in vertical height. Both of these studies measured improved vocal fold edge and supraglottic effort. The scale for true vocal fold edge is 0 to 3, with 0 corresponding to normal, and 3 denoting severely bowed. Supraglottic effort was scaled from 0 to 3, with 0 marking normal and 3 corresponding to severe effort. Crumley et al[13] was the only study to measure mucosal wave changes, with an improvement noted. Vertical height difference and mucosal wave were both set to a scale of 0 to 1, with 0 corresponding to an absence of height difference or

Table 3
Mean phonation time

Study	Intervention	Subjects	MPT (SD) preoperative	MPT (SD) postoperative
Chou*	Primary RLN	8	4.9 (1.3)	10 (1.8)
Miyauchi†	Primary RLN	7	3.95 (2.21)	7.26 (2.68)
Smith‡	Ansa-RLN	6	6.5	13.2
Miyauchi†	Ansa-RLN	63	3.95 (2.21)	7.05 (2.93)
Su*§	Implantation	9	7 (1.22)	16 (5.52)
Paniello	Hypoglossal-RLN	5	2	15.6

MPT, mean phonation time; *SD*, standard deviation; *Primary RLN*, primary recurrent laryngeal nerve anastomosis; *Ansa-RLN*, ansa cervicalis to recurrent laryngeal nerve anastomosis; *Implantation*, ansa cervicalis to thyroarytenoid neural implantation; *Hypoglossal-RLN*, hypoglossal to recurrent laryngeal nerve anastomosis.
*Statistical significance noted for both parameters.
†Phonation efficiency index = MPT/vital capacity.
‡Arytenoid medialization supplementation.
§Medialization thyroplasty supplementation.

abnormal wave, respectively; and 1 representing the presence of a height difference or normal mucosal wave, respectively. Su et al[37] and Maronian et al[42] both noted improvements in muscle atrophy, which was scored as atrophied (0) or intact (1). Two studies[34,37] measured no difference in arytenoid movement, whereas Maronian et al[42] recorded an improvement. Arytenoid movement is scaled at 0 to 2, ranging from asymmetric (0) to normal (2). The scale for vocal fold position is 0 to 3, from normal (0) to lateral (3). This parameter demonstrated mixed findings. Two studies[38,39] measured worsening of vocal fold position, one[37] with improvement, and Maronian et al[42] showing no change. Arytenoid position was scaled from 0 to 3, ranging from symmetric (0) to severely tilted forward (3). Three studies[37-39] were associated with worsening of this parameter.

Perceptual Analysis

Perceptual analysis included patient and professional perceptions of voice and patient perceptions of aspiration (Table 8). Overall grading was scored on a 0 to 3 scale, ranging from poor (0) to excellent (3). Chou et al were the sole reporters of aspiration along with descriptive statistics. The swallowing scale ranged from normal swallowing (0), to severe aspiration (3). All four studies involving patient perceptions of voice[31,35,39,42] noted improvement. Professional overall assessment of voice demonstrated improvement in four studies[34,35,41,43] as well.

Two quantitative scales were used in certain studies: the Grade Roughness Breathiness Asthenia Severity (GRBAS) scale (Table 9), and the Consensus Auditory-Perceptual Evaluation of Voice (CAPE-V) scale which measures severity, roughness, breathiness, and strain (Table 10). GRBAS scales were featured in three studies.[31,33,42] Maronian et al[42] and Chou et al[31] used a scale of 0 to 3, ranging from normal (0) to severe dysphonia (3). Olson et al[33] employed a 0 to 120 scale, with a high score also representing severe dysfunction. Values from Olson were adapted to the aforementioned 0 to 3 scale. All three studies demonstrated improvement for all parameters. However, only Chou et al[31] provided measures of statistical significance for each category. The CAPE-V

Table 4
Shimmer and jitter

Study	Intervention	Subjects	Jitter % (SD) preoperative	Jitter % (SD) postoperative	Shimmer % (SD) preoperative	Shimmer % (SD) postoperative
Zheng*	Ansa-RLN	8	2.03 (1.25)	0.43 (0.23)	8.83 (2.24)	3.22 (2.11)
El-Kashlan†	Ansa-RLN + CT MNM	3	10.6	0.64	1.02	0.15
Su*‡	Implantation	9	2.19 (0.71)	0.54 (0.31)	7.18 (0.97)	2.47 (1.22)
Paniello	Hypoglossal-RLN	5	7.75	0.87	10.5	3.5

SD, standard deviation; *Ansa-RLN*: ansa cervicalis to recurrent laryngeal nerve anastomosis; *CT MNM*, cricothyroid muscle-nerve-muscle neuromuscular pedicle; *Implantation*, ansa cervicalis to thyroarytenoid neural implantation; *Hypoglossal-RLN*, hypoglossal to recurrent laryngeal nerve anastomosis.
*Statistical significance noted for both parameters.
†Injection laryngoplasty with gelfoam and/or arytenoid medialization supplementation.
‡Medialization thyroplasty supplementation.

Table 5
Glottic gap

Study	Intervention(s)	Subjects	Preoperative (SD)	Postoperative (SD)
Chou	Primary RLN	8	2.25 (1.16)	0.5 (0.53)
Zheng	Ansa-RLN	8	2.26	0.75
Lorenz*†‡§	Ansa-RLN; Ansa-RLN + CT MNM	21	0.68	0.19
Lee*	Ansa-RLN; Ansa-RLN + CT MNM	13	1	0.1
Maronian*	Ansa-RLN; NMP	7	1.85	0.28
Su‖	Implantation	9	2	0

SD, standard deviation; *Primary RLN*, Primary recurrent laryngeal nerve anastomosis; *Ansa-RLN*, ansa cervicalis to recurrent laryngeal nerve anastomosis; *CT MNM*, cricothyroid muscle-nerve-muscle neuromuscular pedicle; *NMP*, ansa cervicalis to thyroarytenoid neuromuscular pedicle; *Implantation*, ansa cervicalis to thyroarytenoid neural implantation.
*Injection laryngoplasty supplementation with gelfoam or micronized AlloDerm.
†Preoperative value given as baseline probability of abnormality and postoperative value given as odds ratio of abnormality. Scale not used.
‡Statistical significance noted.
§Confidence interval of 0.04 to 0.9 provided.
‖Medialization thyroplasty supplementation.

scale of normal (0) to severe dysphonia (100) was used in two studies,[38,39] both of which demonstrated improvement in each category.

Electromyography

All studies involving EMG values reported successful reinnervation in all subjects and all muscle targets (Table 11). Positive EMG readings were defined as the presence of at least 20 percent of voluntary motor unit action potentials and recruitment. Two studies[37,42] used the presence of thyroarytenoid action potentials during head lift as further evidence of reinnervation. Likewise, Paniello[40] used tongue protrusion as a means of demonstrating hypoglossal-RLN integrity. No EMG studies were conducted on subjects receiving primary RLN anastomosis. Because of the heterogeneity of the study design, population characteristics, intervention, time of outcome assessment, and method of outcome assessment, it was not possible to perform a meta-analysis.

Discussion

This systematic review reveals that all of the studied reinnervation techniques provide improvement in symptoms to varying degrees based on perceptual, visual, electromyographic, or acoustic outcomes. An association between etiology and the selection of certain procedures is also observed. The most frequently studied technique, ansa-RLN

Table 6
Vertical height difference, true vocal cord edge, supraglottic effort, and mucosal wave

Study	Intervention(s)	Subjects	Preoperative	Postoperative
Vertical height difference				
Lorenz et al*†	Ansa-RLN; Ansa-RLN + CT MNM	21	0.14	0.2
Lee et al*	Ansa-RLN; Ansa-RLN + CT MNM	13	0	0
True vocal fold edge				
Lorenz*†‡	Ansa-RLN; Ansa-RLN + CT MNM	21	0.69	0.25
Lee*	Ansa-RLN; Ansa-RLN + CT MNM	13	1	0.66
Supraglottic effort				
Lorenz*†	Ansa-RLN; Ansa-RLN + CT MNM	21	0.78	1.34
Lee*	Ansa-RLN; Ansa-RLN + CT MNM	13	1.3	0.95
Mucosal wave				
Crumley*§	Ansa-RLN	5	1	0.2

Ansa-RLN, ansa cervicalis to recurrent laryngeal nerve anastomosis; *CT MNM*, cricothyroid muscle-nerve-muscle neuromuscular pedicle.
*Injection laryngoplasty supplementation with gelfoam or micronized AlloDerm.
†Preoperative value given as baseline probability of abnormality and postoperative value given as odds ratio of abnormality. Scale not used.
‡Statistical significance noted with a confidence interval of 0.07 to 0.84.
§Confidence interval of 0.24 to 1.36 provided.

Table 7
Arytenoid position, arytenoid movement, vocal fold position, and thyroarytenoid muscle bulk

Study	Intervention(s)	Subjects	Preoperative	Postoperative
Arytenoid position				
Lorenz*†	Ansa-RLN; Ansa-RLN + CT MNM	21	0.53	0.86
Lee*	Ansa-RLN; Ansa-RLN + CT MNM	13	1	1.1
Su‡	Implantation	9	1.67	3
Maronian*	Ansa-RLN; NMP	7	1	0
Arytenoid movement				
Zheng	Ansa-RLN	8	0	0
Maronian*	Ansa-RLN; NMP	7	0.14	0.43
Su‡	Implantation	9	0	0
True vocal fold position				
Maronian*	Ansa-RLN; NMP	7	2.38	2.38
Lorenz*†	Ansa-RLN; Ansa-RLN + CT MNM	21	0.38	0.33
Lee*	Ansa-RLN; Ansa-RLN + CT MNM	13	1.23	1.13
Su‡	Implantation	9	2.25	2.81
Thyroarytenoid muscle bulk				
Su‡	Implantation	9	0	1
Maronian*	Ansa-RLN; NMP	7	0	1

Ansa-RLN, ansa cervicalis to recurrent laryngeal nerve anastomosis; *CT MNM*, cricothyroid muscle-nerve-muscle neuromuscular pedicle; *Implantation*, ansa cervicalis to thyroarytenoid neural implantation *NMP*, ansa cervicalis to thyroarytenoid neuromuscular pedicle.
*Injection laryngoplasty supplementation gelfoam or micronized AlloDerm.
†Preoperative value given as baseline probability of abnormality and postoperative value given as odds ratio of abnormality. Scale not used.
‡Medialization thyroplasty supplementation.

anastomosis, demonstrated significant improvement in jitter, shimmer, and CAPE-V analysis. Worsening visual findings of supraglottic effort and arytenoid position were not significant. Supplementation of this procedure with CT MNM was associated with high vagal injuries and spinal surgery.

Primary RLN anastomosis was the second-most studied method and was solely associated with thyroid disease

Table 8
Patient and professional perceptions of voice, patient perceptions of aspiration

Study	Intervention(s)	Subjects	Preoperative (SD)	Postoperative (SD)
Patient perceptions of voice				
Chou*	Primary RLN	8	2	3
Smith†	Ansa-RLN	5	0.9	2.55
Maronian‡	Ansa-RLN	5	0	1.4
Lee‡	Ansa-RLN; Ansa-RLN + CT MNM	14	0.6	2.4
Maronian	NMP	3	0	1.67
Professional perceptions of voice				
Smith†	Ansa-RLN	5	1.49	2.39
Zheng	Ansa-RLN	8	0	2.5
Tucker	NMP	73	0	1.9
May‡	NMP	29	0	1.86
Patient perceptions of aspiration				
Chou*	Primary RLN	8	1.125 (0.64)	0.25 (0.46)

SD, standard deviation; *Primary RLN*, Primary recurrent laryngeal nerve anastomosis; *Ansa-RLN,* ansa cervicalis to recurrent laryngeal nerve anastomosis; *CT MNM*, cricothyroid muscle-nerve-muscle neuromuscular pedicle; *NMP*, ansa cervicalis to thyroarytenoid neuromuscular pedicle.
*Statistical significance noted in all parameters.
†Arytenoid medialization supplementation.
‡Injection laryngoplasty supplementation with gelfoam or micronized AlloDerm.

Table 9
Grade, Roughness, Breathiness, Asthenia, Strain (GRBAS) scale analysis

Study	Intervention(s)	Subjects	Preoperative (SD)	Postoperative (SD)
Grade				
Chou*	Primary RLN	8	1.75 (0.71)	0.375 (0.52)
Olson†	Ansa-RLN	11	1.75	1.02
Maronian†	Ansa-RLN	5	2	1.4
Maronian	NMP	3	1.8	0.53
Roughness				
Chou†	Primary RLN	8	1.5 (0.53)	0.5 (0.53)
Olson†	Ansa-RLN	11	3	0.78
Maronian†	Ansa-RLN	5	1.94	1.14
Maronian	NMP	3	1.6	0.67
Breathiness				
Chou*	Primary RLN	8	1.375 (0.74)	0.5 (0.93)
Olson†	Ansa-RLN	11	1.21	0.56
Maronian†	Ansa-RLN	5	1.66	0.66
Maronian	NMP	3	0.9	0.2
Asthenia				
Chou*	Primary RLN	8	1.25 (0.71)	0.125 (0.35)
Olson†	Ansa-RLN	11	1.03	0.64
Maronian†	Ansa-RLN	5	1.48	0.54
Maronian	NMP	3	0.76	0.3
Strain				
Chou*	Primary RLN	8	1 (0.76)	0.25 (0.46)
Olson†	Ansa-RLN	11	0.98	0.91
Maronian†	Ansa-RLN	5	0.06	0
Maronian	NMP	3	0.43	0

SD, standard deviation; *Primary RLN*, primary recurrent laryngeal nerve anastomosis; *Ansa-RLN*, ansa cervicalis to recurrent laryngeal nerve anastomosis; *NMP*, ansa cervicalis to thyroarytenoid neuromuscular pedicle.
*Statistical significance noted in all parameters.
†Injection laryngoplasty supplementation with gelfoam or micronized AlloDerm.

and/or surgery. This approach yielded significant improvement in MPT, GRBAS, patient subjective aspiration ratings, and patient subjective voice perception. Patients undergoing NMP were associated with similar etiologies as those undergoing ansa-RLN with or without CT MNM. In particular, mediastinal tumors and spinal surgery was a more prevalent cause of UVFP in these populations. This technique demonstrated positive outcomes in terms of visual, percep-

Table 10
Consensus Auditory-Perceptual Evaluation of Voice (CAPE-V) scale analysis

Study	Intervention(s)	Subjects	Preoperative (SD)	Postoperative (SD)
Severity				
Lee*	Ansa-RLN; Ansa-RLN + CT MNM	13	100	35
Lorenz*†	Ansa-RLN; Ansa-RLN + CT MNM	21	61.3 (5.6)	37.9 (7.3)
Roughness				
Lee*	Ansa-RLN; Ansa-RLN + CT MNM	13	100	30
Lorenz*†	Ansa-RLN; Ansa-RLN + CT MNM	21	41.4 (5.3)	23.1 (7.1)
Breathiness				
Lee*	Ansa-RLN; Ansa-RLN + CT MNM	13	100	0
Lorenz*†	Ansa-RLN; Ansa-RLN + CT MNM	21	53.3 (6)	43.8 (8)
Strain				
Lee*	Ansa-RLN; Ansa-RLN + CT MNM	13	100	66
Lorenz*†	Ansa-RLN; Ansa-RLN + CT MNM	21	24.7 (5.6)	15.6 (7.4)

SD, standard deviation; *Ansa-RLN*, ansa cervicalis to recurrent laryngeal nerve anastomosis; *CT MNM*, cricothyroid muscle-nerve-muscle neuromuscular pedicle.
*Injection laryngoplasty supplementation with gelfoam or micronized AlloDerm.
†Statistical significance noted in all parameters.

Table 11
Electromyography

Study	Intervention	n	TA Preoperative	TA Postoperative	TA Active with head lift	CT Preoperative	CT Postoperative
Maronian*	Ansa-RLN	2	All inactive	All active	Present	–	–
Zheng	Ansa-RLN	3	All inactive	All active	–	–	–
El-Kashlan†	Ansa-RLN + CT MNM	3	All inactive	All active	–	All inactive	All active
Maronian	NMP	2	All inactive	All active	Present	All active	All active
Su‡	Implantation	4	All inactive	All active	Present	–	–
Paniello	Hypoglossal-RLN	5	All inactive	All active	–	–	–

TA, thyroarytenoid muscle; *CT*, cricothyroid muscle; *Ansa-RLN*, ansa cervicalis to recurrent laryngeal nerve anastomosis; *CT MNM*, cricothyroid muscle-nerve-muscle neuromuscular pedicle; *active*, presence of at least 20% voluntary motor unit action potentials and recruitment; *NMP*, ansa cervicalis to thyroarytenoid neuromuscular pedicle; *Implantation*, ansa cervicalis to thyroarytenoid neural implantation; *Hypoglossal-RLN*, hypoglossal to recurrent laryngeal nerve anastomosis.
*Injection laryngoplasty supplementation with gelfoam.
†Medialization and/or injection laryngoplasty.
‡Medialization thyroplasty supplementation.

tual, subjective, and electromyographic assessments. In particular, improvement in arytenoid position contrasts with the worsening observed in ansa-RLN. However, both techniques failed to show significance in this category.

Only a single study[37] measured the effects of the implantation technique on outcome, with the majority of subjects from thyroid and spinal surgery. Although this method did demonstrate significant improvements in MPT, shimmer, and jitter, there was an insignificant worsening in TVC and arytenoid position. The hypoglossal anastomosis technique was studied in a single study.[40] The majority of these cases were associated with mediastinal masses and idiopathic causes. One reason for this relationship may have been the availability of more familiar donor nerves (RLN, ansa cervicalis, etc.) for paralysis related to thyroid disease/surgery. Paniello[40] performed preoperative injections to the hypoglossal with no impact on swallowing and articulation in an effort to address possible morbidity related to this procedure.

There are several weaknesses that exist within this study. First, the methodologic quality of the design and report of most of the included studies was lacking. As reflected in our quality checks, deficiencies existed in multiple studies in regards to data acquisition purposes, follow-up, sampling methods, and accounts of missing data. Only four[31,35,37,38] of the 14 articles reported on the statistical significance of their findings. Second, as is typical with systematic reviews, there was heterogeneity between different studies using the same reinnervation method in terms of outcome parameters, follow-up periods, observation periods before reinnervation, and the use of supplemental medialization procedures.

Although there were possible deficiencies observed in terms of supraglottic effort and arytenoid position for the ansa-RLN method, these parameters were not measured in patients who underwent primary RLN, precluding direct comparison. All patients undergoing supplemental temporary laryngoplasty injection received either gelfoam or micronized AlloDerm, which are reported to last approximately six to 12 months[11] and eight to 12 weeks,[12] respectively. With our observed range of two to 12 months before clinical signs of reinnervation, interference with outcomes is a possibility. A third limitation was the pooling of multiple techniques in the reporting of preoperative data and/or outcomes within a single study. Miyauchi et al combined the preoperative data from their ansa-RLN and primary RLN subjects. Maronian et al[42] pooled data on the visual analysis of NMP and ansa-RLN patients. Lee et al[39] and Lorenz et al[38] failed to differentiate data between patients that underwent ansa-RLN versus ansa-RLN combined with CT MNM. Fourth, although aspiration is a reported complication of UVFP with considerable morbidity,[1] only Chou et al[31] chose to address this issue. Furthermore, with the potential risks of an open neck procedure performed under general anesthesia, Miyauchi et al[32] was the sole author to specifically mention the lack of any complications including hematomas, wound breakdown, or infection. The fifth and perhaps most clinically relevant limitation is that, with the exception of Chou et al,[31] most repairs took place several months to years after the initial surgical procedure. As stated previously, one of the major advantages of reinnervation is the ability to immediately address nerve injury intraoperatively, potentially circumventing future surgical procedures.

Synkinesis is a proposed complication of RLN damage or repair. This phenomenon is thought to result from aberrant reinnervation of adductor/abductor fibers. Crumley[7] has suggested a classification scheme: type I with vocal fold poorly mobile or immobile; type II with spasmodic vocal folds; type III with hyperadducted vocal folds; and type IV with hyperabducted vocal folds and possible aspiration. Without a preoperative categorization or specific identification of synkinesis, associating the worsening of supraglottic effort and arytenoid position following ansa-RLN with postoperative synkinesis is not possible. These same deficiencies preclude an association between repair and abatement of synkinesis for positive visual findings. This may be one area of interest for future study.

Conclusion

Although all of the observed reinnervation techniques demonstrate positive effects on UVFP in terms of acoustic, perceptual, electromyographic, and visual outcomes, the quality of the current literature is low. Heterogeneity in the available literature prevented us from not only performing a meta-analysis, but making direct comparisons between techniques as well. Although valid recommendations for specific methods are not feasible at this time, the association between certain etiologies or anatomical limitations and the choice of reinnervation technique is noted. We therefore believe that prospective studies, preferably in the setting of immediate intraoperative repair, should be initiated using uniform and consistent outcome parameters.

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Behrad B. Aynehchi, conception and design, acquisition of data, analysis and interpretation of data, drafting article, and final approval of version to be published; **Edward D. McCoul,** design, acquisition of data, revising article critically for important intellectual content, and final approval of version to be published; **Krishnamurthi Sundaram,** conception and design, revising article critically for important intellectual content, and final approval of version to be published.

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