Innervation Status in Chronic Vocal Fold Paralysis and Implications for Laryngeal Reinnervation

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INTRODUCTION

Treatment options for symptomatic unilateral vocal fold paralysis (VFP) include vocal fold augmentation, laryngeal framework surgery, and laryngeal reinnervation procedures. Laryngeal reinnervation (LR) is thought to preserve or provide thyroarytenoid-lateral cricoaryte- 

Objective: Treatment options for symptomatic unilateral vocal fold paralysis (VFP) include vocal fold augmentation, laryngeal framework surgery, and laryngeal reinnervation. Laryngeal reinnervation (LR) has been suggested to provide “tone” to the paralyzed VF. This implies a loss of tone as a result of denervation without reinnervation. We performed laryngeal electromyography (LEMG) in patients with chronic VFP to understand the innervation status associated with a chronically paralyzed vocal fold.

Study Design: Retrospective review of LEMG data in adult patients with chronic VFP from January 2009 to December 2014.

Methods: LEMG was performed at least 6 months after-onset of VFP. Qualitative LEMG, quantitative LEMG, and adduc- 

tory synkinesis testing were performed, and the parameters were collected.

Results: Twenty-seven vocal folds were studied (23 unilateral VFP and 2 bilateral VFP). Average age was 59 ± 17 years. The median duration from recurrent laryngeal nerve injury to LEMG was 8.5 months (range 6–90 months). The majority of patients, 24 of 27 (89%), had motor unit potentials during phonation tasks on LEMG, and only 3 of 27 (11%) patients were electrically silent. Quantitative LEMG showed 287.8 mean turns per second (normal ≥ 400). Motor unit configuration was normal in 12 of 27 (44%), polyphasic in 12 of 27 (44%), and absent in the electrically silent patients. Adductory synkinesis was found in 6 of 20 (30%) patients.

Conclusion: Chronic vocal fold paralysis is infrequently associated with absent motor-unit recruitment, indicating some degree of preserved innervation and/or reinnervation in these patients. LEMG should be part of the routine workup for chronic VFP prior to consideration of LR.

Key Words: Chronic vocal fold paralysis, vocal fold paralysis, vocal cord paralysis, EMG, LEMG, laryngeal electromyography, laryngeal reinnervation.

Level of Evidence: 4.

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Recent advances in LEMG have allowed quantitative analysis of the interference pattern using turns analysis, which is a validated methodology in EMG. The normal threshold for TA-LCA muscle complex is found to be more than a mean of 400 turns per second, determined by normative data from turns analysis from a cohort of health controls. The addition of quantitative LEMG analysis to standard analysis of motor unit recruitment and configuration allows patient categorization into excellent, fair, and poor prognosis of vocal fold motion recovery depending on LEMG findings. Further, adductor synkinesis can be identified electromyographically by measuring the electrical activities of the TA-LCA muscle complex during phonation and during a sniff task. Contrary to the traditional view that any adductor activity during a sniff qualifies as synkinesis, the TA muscle was found to be active on inhalation during rapid breathing and during a sniff in a landmark LEMG study conducted by Hillel. In the same study, the LCA and interarytenoid were also found to be active during sniffing in some patients. As a result, adductor synkinesis is defined in the literature as TA recruitment during a sniff that is greater than or equal to its recruitment during phonation. This definition highlights the markedly abnormal activity of the TA-LCA during a sniff task while accounting for their normal laryngeal activities. The senior authors’ (L.J.S., M.C.M., C.A.R.) previous study further quantifies this definition on LEMG; therefore, adductor synkinesis is determined to be present if the TA-LCA motor unit potential amplitude ratio during a sniff and during phonation is greater than 0.65. The presence of adductor synkinesis on LEMG will downgrade a patient’s prognosis for vocal fold motion recovery to the poor category but has been found to result in improved voice outcomes. The combination of qualitative information, quantitative analysis, and adductor synkinesis testing has improved the positive predictive value, negative predictive value, and prognostic accuracy of LEMG to 100%, 90%, and 91%, respectively.

As mentioned previously, LR has been proposed to not restore motion, but to provide tone to the paralyzed VF. This implies a loss of tone due to denervation. Animal studies have shown that complete denervation in laryngeal muscles is rare after RLN injury. Zealer et al. cited unpublished EMG data from paralyzed TA muscle during thyroplasty, which found evidence of reinnervation in 17 of 20 (85%) patients at least 6 months after RLN injury. However, EMG findings in a chronically paralyzed vocal fold (> 6 months from onset of RLN injury) have never been formally reported in the literature. Therefore, the objective of the current study is to investigate and describe LEMG findings in chronic VF to understand the innervation status of the chronically paralyzed vocal fold.

**Materials and Methods**

**Study Design and Subjects**

This study was approved by the institutional review board (IRB) at the University of Pittsburgh (IRB PRO13090372). A retrospective review was performed on adult patients with permanent unilateral or bilateral VFP of a peripheral neurogenic etiology who had undergone diagnostic LEMG at least 6 months from the onset of RLN injury between January 2009 to December 2014. All patients had an endoscopic laryngeal examination 6 months after onset of injury to ensure persistent VFP. Those with vocal fold motion recovery, vocal fold immobility secondary to cri-coarytenoid joint fixation based on LEMG, unclear onset of RLN injury, and LEMG performed within 6 months of RLN injury were excluded. In addition to chart review, we also contacted patients known to have chronic VFP by telephone to return to the clinic to participate in an elective diagnostic LEMG.

**Electromyography Method**

The laryngeal electromyogram was performed by two fellowship-trained laryngologists (L.J.S., C.A.R.). A board-certified electrodiagnostic medicine physician (M.C.M.) was also present to interpret the data. The physician performing as well as the one interpreting the data were blinded to the laterality of the patient’s vocal fold paralysis. Only information regarding the onset of injury, past medical history, and past surgical history were known to the electrodiagnostic physician at the time of LEMG testing. A Synergy T5EP NCS EMG machine (Natus Neurology, Middleton, WI) was used, recording motor unit recruitment tracings in synchronization with a surface microphone tracing. All patients received either 0.5 mL injection of a 50:50 mixture of 1% lidocaine with 1:100,000 epinephrine and bicarbonate or 3 mL of EMLA Cream 5% (Eutectic Mixture of Local Anesthetics, 2.5% lidocaine and 2.5% prilocaine, AstraZeneca, Macclesfield, Cheshire, UK) over the cricothyroid membrane. A 37-mm concentric needle electrode was utilized in conjunction with a ground electrode placed over the wrist. The concentric needle was inserted through the cricothyroid membrane to locate the TA-LCA muscle complex. The TA and LCA muscles were not tested separately, but rather the entire TA-LCA muscle complex was tested, the rationale being that the LCA muscle is in close proximity to the TA muscle and often contributes to the activity recorded from the TA, particularly when a monopolar electrode is used. After insertion, needle position was confirmed by asking patients to perform both a sustained vowel /i/ phonation and a Valsalva maneuver. For spontaneous activity, a sweep speed of 10 msec per division and a gain of 50 μV per division were used. For motor unit analysis, sweep speed was the same, but gain was changed to 200 μV per division. Adductory synkinesis testing was performed on all patients who demonstrated normal or mildly to moderately decreased recruitment (1+ to 2+). The LEMG methodology used for grading motor unit recruitment using an ordinal scale has been previously described; it ranges from 4+ or absent recruitment to 1+ or mildly decreased activation based on the number of units on the screen and the firing rate of the fastest unit. Synkinesis testing and quantitative analysis were not performed in patients with severely decreased (3+) or absent (4+) recruitment because too few motor units were firing to measure for possible abnormal reinnervation and for turns analysis. Adductory synkinesis testing was performed by asking the patient to produce a sustained /i/ at maximal intensity for approximately 3 seconds, briefly pause, and then quickly sniff. Synkinesis was determined to be present if the ratio of sniff:phonation motor unit potential amplitude was greater than 0.65.

**Outcomes and Analysis**

Eligible subjects’ medical records were reviewed. In addition, we called patients in the institution database with known diagnosis of permanent vocal fold paralysis and asked whether they would be willing to undergo an LEMG. Age, etiology and...
**Qualitative and Quantitative LEMG Analysis**

<table>
<thead>
<tr>
<th>Pt No./Sex/Age, yr</th>
<th>Etiology of VFP</th>
<th>VHI-10 Scores at Diagnostic LEMG</th>
<th>Qualitative LEMG Analysis</th>
<th>Quantitative LEMG Analysis</th>
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<tr>
<td>1/F/58</td>
<td>Idiopathic</td>
<td>36</td>
<td>None fired</td>
<td>245 N/A Positive</td>
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<tr>
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<td>26</td>
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<td>None fired</td>
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<tr>
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<td>None fired</td>
<td>218 0 Negative</td>
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<tr>
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<td>3</td>
<td>None fired</td>
<td>487 &gt;3 Positive</td>
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<td>Malignant invasion</td>
<td>40</td>
<td>None fired</td>
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<tr>
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<td>None fired None fired N/A</td>
</tr>
<tr>
<td>25/F/77</td>
<td>Idiopathic</td>
<td>22</td>
<td>None fired</td>
<td>267 0 Positive</td>
</tr>
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</table>

**Patients** 18 and 19 had bilateral vocal fold paralysis; thus, each vocal fold is presented in the table separately.

**Results**

Nineteen patients met the inclusion criteria from chart review. An additional six patients returned to the clinic voluntarily for an elective diagnostic LEMG; therefore, a total of 25 patients were included in this study. Twenty-seven vocal folds were investigated, including 23 unilateral VFP and 2 bilateral VFP. Average age was 59 ± 17 years. The study cohort was predominantly female (22 of 25 patients). Etiologies of VFP included idiopathic (40%, 10 of 25), iatrogenic (56%, 14 of 25), and malignant invasion (4%, 1 of 25) (Table I). The median time between RLN injury and LEMG was 8.5 months (range 6–90 months). For patients with unilateral VFP, the average VHI-10 score around the time of the diagnostic LEMG was 19.6 ± 10.9 (maximum score = 40), and 22% of these were within the normal range (VHI-10 score ≤11). For the two patients with bilateral VFP (patient 18 and 19), baseline VHI-10 scores were 10 and 0, respectively.

On qualitative LEMG analysis, 24 of 27 (89%) vocal folds had motor unit potentials in the TA-LCA muscle complex during phonation tasks on LEMG, and three of 27 (11%) vocal folds were electrically silent (Table I:...
patients 4, 5, and 24). Motor unit configuration was normal in 12 of 27 (44%), polyphasic in 12 of 27 (44%), and absent in the electrically silent patients. Excluding those who were electrically silent, quantitative LEMG data were available in 20 of 24 (83%) vocal folds. The mean value was 287.8 mean turns per second (normal ≥400). Quantitative LEMG data from available patients were graphically presented in Figure 1. Adductory synkinesis testing was performed in 20 patients, which was positive in 6 individuals (30%). Ten of 25 (40%) patients ultimately underwent permanent vocal fold augmentation procedures after diagnostic LEMG (medialization laryngoplasty with or without arytenoid adduction or vocal fold lipoinjection). The median time between permanent vocal fold medialization procedure and onset of RLN injury was 9.9 months (range 5–89 months).

**DISCUSSION**

The current study confirmed that nearly 90% of chronically paralyzed vocal folds maintained some degree of persistent innervation and/or reinnervation. The amount of innervation appeared to be substantive on turns analysis on LEMG (Fig. 1). The 11% incidence of electrical silence reported in the current series is within what has been reported in the literature. Adductor synkinesis was positive in 30% of the current study cohort, which is comparable to previously reported incidences in the literature. The median time between RLN injury and LEMG was 8.5 months in this study, which represents a reasonable interval to detect reinnervation. The findings suggest that complete laryngeal muscle denervation is infrequent, and there remains a significant amount of laryngeal innervation to the TA-LCA muscle complex to maintain laryngeal muscle tone in a large majority of patients with permanent VFP.

The goal of LR is not to restore vocal fold motion but to provide vocal fold muscle tone and maintain the bulk of laryngeal muscles. The current study found that 89% of chronically paralyzed vocal folds had some degree of innervation, which means that vocal fold muscle tone is maintained through natural reinnervation following RLN injury. Therefore, there is likely no need to attempt to restore the innervation by performing LR. To further support this, individuals with electromyographic evidence of adductor synkinesis have been shown to have reduced perception of voice handicap, as measured by the VHI-10, and are less likely to require permanent vocal fold augmentation compared to those without synkinesis, presumably due to the maintenance of laryngeal muscle tone and therefore medialization of the paralyzed vocal fold. Lastly, it is important to consider the natural history of vocal fold paralysis prior to consideration of permanent vocal fold augmentation. In the current study cohort of patients with chronic unilateral VFP, approximately 22% were asymptomatic, that is, with normal VHI-10 scores at the time of LEMG and thus negating the need for additional interventions. This finding was consistent with a previous report that 20% of patients reported normal perception of voice handicap despite persistent vocal fold paralysis.

Spontaneous laryngeal muscle reinnervation is a complicated process due to the complexity of intralaryngeal neuroanatomy and is not well understood. In addition to the traditional thought of the larynx being solely innervated by superior laryngeal nerve (SLN) and RLN, other neural connections such as the Galen's anastomosis, the human communicating nerve, and the interarytenoid neural plexus have been identified through recent anatomic studies. Following injury to the RLN, it is likely that the preserved axons will expand their territories and reinnervate the intralaryngeal muscles through collateral sprouting. Other evidence has also suggested that intrinsic laryngeal muscles are not innervated by RLN alone. Dual innervation of the TA, LCA, and posterior cricoarytenoid muscles from both the SLN and RLN has been demonstrated in pigs. In addition, an immunohistochemistry study performed in rats has shown that the SLN acts as a source of reinnervation for TA muscle following RLN injury. The resulting reinnervation may be inadequate, inappropriate, or
nonexistent. Hence, without performing a baseline LEMG, it is impossible to know the innervation status of a chronically paralyzed vocal fold and anticipate whether LR can provide additional benefit for the patients.

Age has been suggested as an influential factor for LR outcomes. A large retrospective series consisted of 349 unilateral VFP patients who underwent LR.31 This study showed that patients under age 60 did better in postoperative outcomes such as glottal closure, shimmer, and noise-to-harmonics ratio compared to those over age 60. A recent systematic review on surgical interventions for pediatric unilateral VFP suggested that LR is likely a better option in this population despite a lack of long-term follow-up data.32 Laryngeal reinnervation is performed under general anesthesia, which is more ideal in children who likely will not tolerate laryngeal framework surgery under monitored anesthesia care. In addition, the preservation of laryngeal anatomy allows for unaltered development and growth of the thyroid cartilage as the child matures. Although this systematic review finds that LR may be a better option for younger patients, LEMG data in the pediatric population are critically lacking; therefore, it is unknown whether children with chronically paralyzed vocal folds maintain some degree of persistent innervation. Future studies involving LEMG should be considered so we can shed light on laryngeal innervation status in the pediatric population with permanent VFP.

In adults with chronic VFP, however, LR may not be a preferred option compared to static medialization procedures. A randomized clinical trial directly compared medialization laryngoplasty (ML) and LR using ansa cervicalis to RLN anastomosis in patients with permanent unilateral VFP.33 This study included 12 patients per group. Of all the LR patients who had preoperative and postoperative LEMG data, six had unchanged LEMG findings, whereas five had “improvement” by one or more classes and one declined by one class based on the Koufman and Walker’s EMG classification.34 Patients who were electrically silent before LR all regained some interference pattern after the surgery. Of the ML group, six of 12 patients had preoperative and postoperative LEMG data, with four having unchanged LEMG findings and two improved by one class. Neither group had significant changes in any of the major outcome parameters, including perceptual voice rating, Voice-Related Quality of Life scores (V-RQOL), and GRBAS scores. The LR group failed to demonstrate better results than the ML group at 12 months, suggesting that these two surgical techniques have comparable long-term voice results. Subgroup analysis using age showed that younger LR patients were better than the younger ML patient at 12 months in GRBAS scores but not in perceptual voice rating and V-RQOL scores. However, this study was underpowered. As a result, one cannot draw definitive conclusions from this finding, and whether younger LR patients truly do better than younger ML patients in the long run remains to be determined. Outcomes of LR and ML for unilateral VFP in adults are further summarized and compared by a systematic review. This study found that LR had a delayed benefit in voice outcome, with maximal benefit reached several months after surgery, whereas benefits from ML were almost immediate.35 The authors proceeded to suggest that the marginal benefits from LR compared to other medialization techniques might not outweigh the technical challenges that LR surgery presents. Therefore, LEMG should be a major component of the selection process for consideration of LR in order to identify VFP patients with electrical silence during phonation, who would most likely benefit from reinnervation procedures.

There are several important factors that are involved in the diagnostic accuracy of LEMG, including correct needle placement, standardized LEMG techniques, as well as minimization of interpretation bias. The most obvious of confounding variables for explaining decreased LEMG accuracy is mistaken needle placement during the exam. The accuracy of needle placement was confirmed by correct identification of anatomic landmarks, and demonstration of insertional activities as well as interference pattern on appropriate phonatory tasks. Adductor synkinesis testing and quantitative LEMG protocols have been standardized at the study institution; therefore, every exam was performed the same way by the electromyographer. In addition, quantitative LEMG methodology is very sound through automation. The electromyographer samples 10 milliseconds epochs, and the computer software automatically calculates the mean turns per second. Electrical activity tracings are only sampled with sharp motor unit rise time, which is indicated by a green color on a quality control meter on the LEMG machine. To minimize interpretation bias, the laryngologist inserting the EMG needle was not the patient’s primary treating laryngologist, and the electromyographer only collected limited history prior to the exam. By addressing the aforementioned factors in the LEMG protocol, we were confident in our findings regarding the innervation status of chronically paralyzed vocal folds.

One limitation of this study was that it was a retrospective review; therefore, the results relied on the completeness and accuracy of the medical records. Strict inclusion criteria made our findings representative of LEMG characteristics in a cohort of patients with permanent VFP. A second limitation was the small sample size; however, this was the largest LEMG cohort with chronic VFP that we know of in the literature, and our findings were comparable to previously cited unpublished data.16

We found that about 90% of the chronically paralyzed vocal folds remain persistently and substantially innervated. This finding suggests that a preoperative LEMG is imperative in clinical decision making regarding candidacy for LR. An otolaryngologist or laryngologist can collaborate with an electromyographer for performing and interpretation of LEMG using the protocol outlined in the current study. If a patient has a substantive amount of recruitment based on quantitative LEMG, LR may not provide any additional benefit. However, if a patient has minimal or no recruitment on
LEMG, LR may be performed to restore TA-LCA muscle tone for better voice outcome. Further research should focus on quantification of the amount of recruitment that will be required for maintaining vocal fold muscle tone, or even for restoration of vocal fold motion. Furthermore, a direct comparison of long-term voice outcomes between those with some electrical activities on LEMG and those with no electrical activities on LEMG undergoing LR should be performed.

CONCLUSION
Vocal fold paralysis is uncommonly associated with complete denervation of laryngeal muscles. About 90% of patients with chronic VFP in the current study showed some degree of persistent innervation and/or reinnervation. LEMG should be a part of the routine workup for permanent VFP prior to consideration of LR given the small incidence of complete absence of electrical activities in a chronically paralyzed vocal fold. Laryngeal reinnervation may be best suited for patients who are electrically silent.

BIBLIOGRAPHY