Selective Cricothyroid Muscle Reinnervation by Muscle-Nerve-Muscle Neurotization

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Objective: To determine if selective reinnervation of the cricothyroid muscle could be achieved with muscle-nerve-muscle neurotization.

Design: Case series.

Setting: Tertiary referral center.

Patients: Three consecutive patients with high vagal lesions that resulted in unilateral laryngeal paralysis.

Interventions: Patients underwent laryngeal reinnervation with ansa hypoglossi to recurrent laryngeal nerve anastomosis. In addition, patients underwent selective cricothyroid muscle reinnervation by muscle-nerve-muscle neurotization technique.

Main Outcome Measures: Objective and subjective improvement in voice quality and electromyographic evidence of selective reinnervation of the cricothyroid muscle.

Results: All patients recovered normal or near-normal speaking voice and had normal objective measures of voice quality. They also showed electromyographic evidence of cricothyroid muscle reinnervation.

Conclusion: The muscle-nerve-muscle neurotization technique was successful in providing selective reinnervation of the cricothyroid muscle in our 3 patients.


It is universally accepted that expeditious movement- and temporal-specific reinnervation is the treatment of choice following denervation of skeletal muscle in the head and neck. This goal has been elusive in our efforts to provide optimal rehabilitation for patients with laryngeal paralysis.

When skeletal muscles are denervated, the method of reinnervation has a major impact on the structure and function of the target skeletal muscle. Several types of reinnervation exist. Direct reinnervation results in superior recovery of contractile function and is the preferred option when available. Examples include primary nerve repair and nerve grafting. Neural neurotization is a second type of reinnervation and involves implantation of the transected motor nerve directly into the target muscle belly. Direct nerve implant and nerve-muscle pedicles are examples of neural neurotization. Muscle-to-muscle neurotization is a third type and occurs when axons sprout from an adjacent, innervated skeletal muscle to innervate a target denervated muscle. The latter types of reinnervation typically result in diminished recovery of contractile function when compared with direct reinnervation.

Muscle-to-muscle neurotization was first used in facial reanimation in the early 1970s. Small muscles were transplanted without vascular anastomosis and positioned adjacent to the muscle bellies of innervated, functional facial muscles. Thompson1,2 demonstrated, first in dogs and later in humans, a degree of functional recovery in these muscle grafts. Carlson and Faulkner3 demonstrated that the force of contraction of such grafts may only be 20% of the original muscle. Hake-Ilius4 described 28 patients with facial paralysis treated by this technique. Twenty-three of these patients developed marked improvement in facial symmetry and motion.

Muscle-nerve-muscle neurotization builds on the principles demonstrated by these investigators. One end of an autogenous nerve graft is placed into the belly of a donor (innervated) muscle, and the other end into a target (denervated) muscle. Axons sprouting from the donor

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MATERIALS AND METHODS

Three patients with high vagal lesions are the subjects of this report. The procedures were performed after detailed discussion and informed consent was obtained. Patients were candidates for and underwent a contralateral ansa hypoglossi–to–ipsilateral RLN anastomosis. In addition, selective cricothyroid reinnervation was attempted using the muscle-nerve-muscle neurotization technique. A segment of peripheral nerve long enough to span between the cricothyroid muscles was harvested from the ansa hypoglossi. One end of the graft was buried in the belly of the innervated cricothyroid muscle and the other end was buried in the denervated side. The graft was secured at the point of entry into each muscle using fine suture from epineurium to muscular fascia. Patient 1 had 2 such grafts placed. Patients underwent videostroboscopic examination of the larynx and perceptual and acoustic analysis of voice preoperatively and at multiple postoperative intervals.

RESULTS

CASE 1

A 45-year-old woman was referred with the chief complaint of a persistent right-sided oropharyngeal mass noted following an upper respiratory tract infection. She also complained of right-sided otalgia and mild neck stiffness, but had no voice or swallowing complaints. Physical examination was remarkable for an approximately 2.5 × 3-cm right oropharyngeal mass covered by mucosa and centered in the tonsillar fossa. Cranial nerve examination was grossly normal except for mild incidental right lip weakness. A computed tomographic (CT) scan of the neck and angiography demonstrated a vascular mass in the right prestyloid parapharyngeal space consistent with a glomus tumor and a right-sided thyroid nodule. A multiple endocrine neoplasia syndrome was ruled out. The patient subsequently underwent embolization of feeding vessels followed by transcervical resection of the tumor.

Surgical findings included a 4 × 2-cm vascular mass surrounding the vagus nerve and close association of the mass with cranial nerve XII. The vagus nerve was cut to remove the tumor, and the findings of the pathologic examination were consistent with a vagal paraganglioma. The patient’s voice was severely breathy postoperatively, consisting essentially of only audible air escape, and she required enteral nutrition via a nasogastric tube for 3 months. Four months postoperatively, a laryngeal electromyogram (EMG) demonstrated electrical silence in the atrophic right thyroarytenoid muscle, and her voice remained severely breathy. The results of acoustic voice assessment were grossly abnormal, with jitter of 20.50% and shimmer of 1.85 dB. One month later, she underwent laryngeal reinnervation with a contralateral ansa hypoglossi–to–ipsilateral RLN anastomosis and a muscle-nerve-muscle reinnervation of the ipsilateral cricothyroid muscle using 2 cable grafts spanning from the contralateral cricothyroid muscle. An injection of the right vocal fold with an absorbable gelatin sponge (Gelfoam) and a right hemithyroidectomy were also performed at the same time.

Postoperatively, the patient’s voice was initially much improved, but was breathy again by 6 weeks after the injection with the absorbable sponge and reinnervation. At approximately 2 months after reinnervation, she felt that her voice strength again began to improve, and by 4 months it was only mildly breathy. Laryngeal videostroboscopy at that time showed good glottic closure in mid- and lower-pitch ranges and incomplete closure in her upper range. A laryngeal EMG was performed at 7 months after reinnervation. The intact, donor cricothyroid muscle was stimulated transcutaneously using a bipolar needle electrode. Recording from the reinnervated cricothyroid muscle was accomplished using a concentric needle electrode. This demonstrated compound potentials (M-wave potentials) in the reinnervated cricothyroid muscle with stimulation of the contralateral donor muscle (Figure 1B) and confirmed reinnervation of the right thyroarytenoid muscle. Activity in the reinnervated cricothyroid muscle was also demonstrated with high-pitched vocal tasks (Figure 1C). The results of acoustic analysis 7 months postoperatively were within normal limits, with jitter of 0.88% and shimmer of 0.17 dB. The patient’s maximum phonation time for a sustained vowel was 12 seconds, and perceptual speaking voice quality was normal except for hypernasal resonance.

CASE 2

A 41-year-old woman presented with a 2-year history of a slow-growing, right-sided neck mass and hoarseness. The results of physical examination were remarkable for a 4 × 3-cm, right-sided neck mass behind the angle of the mandible. There was a medial bulge of the right lateral oropharyngeal wall, which extended superiorly into the nasopharynx. Right true vocal fold (TVF) movement was sluggish. Both CT and magnetic resonance imaging scans were obtained and showed a large vascular right parapharyngeal space mass consistent with a paraganglioma. Carotid angiography demonstrated a large, extremely vascular mass with significant anterior displacement of the internal carotid artery compatible with a glomus vagale tumor. The identifiable blood supply to the tumor was embolized. The patient was taken to the
operating room the next day and underwent excision of the tumor through a mandibular swing approach. Tumor extirpation required interruption of cranial nerves IX, X, XI, and XII. Postoperatively, the patient had dysphagia and an immobile right TVF, resulting in extreme breathiness and poor projection, which did not improve for 6 months. Acoustic voice analysis showed a jitter of 0.75% and shimmer of 0.19 dB.

Six months following resection, the patient was taken to the operating room, where she underwent direct laryngoscopy and laryngeal EMG. These procedures demonstrated an absence of motor unit potential activity in the right thyroarytenoid muscle, whereas the left thyroarytenoid muscle had normal motor unit potential recruitment synchronized with the patient’s spontaneous respiration. The cricothyroid muscle showed no motor unit potentials on the right side, whereas the left side was normal. The patient underwent laryngeal reinnervation by left ansa hypoglossi–to–right RLN anastomosis. A muscle-nerve-muscle graft was performed from her functional left cricothyroid muscle to the nonfunctional right cricothyroid muscle. An injection with an absorbable gelatin sponge (Gelfoam) was also given.

Approximately 3 months after surgery, the patient noticed gradual improvement of her vocal quality. There was a significant improvement in terms of voice strength and projection between 4 and 5 months after surgery. Initial stroboscopic examination before laryngeal reinnervation showed the paralyzed right TVF to be in the intermediate position with incomplete closure of the glottis during phonation. The TVFs were at a slightly different vertical level, which contributed to the inadequacy of glottic closure. Postreinnervation stroboscopy at 6 months showed the right TVF to be in the midline with adequate glottic closure, except for a very small posterior gap, which was clinically insignificant. The right TVF had good bulk and tone and was at the same vertical level of the normal left fold. The patient considered her voice to be normal with an almost normal frequency range. The results of acoustic analysis 8 months postoperatively were within normal limits, with jitter of 0.39% and shimmer of 0.14 dB. Her perceptual speaking voice quality was normal, except for hypernasal resonance. Figure 2 shows the prereinnervation and postreinnervation EMG tracings from cricothyroid muscles, confirming reinnervation of the right cricothyroid muscle.

**CASE 3**

A 26-year-old man presented with a high, left-sided neck mass. Appropriate workup was performed, and the mass was consistent with a large glomus vagale extending from...
the jugular foramen to C3. Carotid angiography was performed. Carotid occlusion studies and tumor embolization were performed. The patient then underwent excision of the tumor with division of cranial nerve X. Because of anticipated dysphagia from the interruption of cranial nerve X, type 1 thyroplasty was performed to facilitate glottic closure and postoperative swallowing. He also underwent primary laryngeal reinnervation with a contralateral ansa hypoglossi to ipsilateral RLN anastomosis and muscle-nerve-muscle reinnervation of the ipsilateral denervated cricothyroid muscle using a nerve cable graft from the normal innervated contralateral cricothyroid muscle.

Postoperatively, the patient’s voice was rough and raspy with significant problems with projection and pitch control. He was only able to speak 1 to 3 words per breath. Videolaryngoscopy showed the paralyzed left TVF to be in the paramedian position with incomplete closure of the glottis during phonation. Approximately 4 months postoperatively, the patient reported gradual improvement of his voice, with increase in phonation time and increased projection. The patient also noted significant increase of his pitch range, and he described his voice as being completely normal approximately 6 months postoperatively. Videolaryngoscopic examination at that time showed the paralyzed left TVF to be in the midline with complete glottic closure during phonation. Both vocal folds were at the same vertical level and had similar bulk. The EMG recordings showed reinnervation of the left cricothyroid muscle with some normal configuration motor unit potentials at rest and recruitment with phonation (Figure 3). The results of acoustic analysis 6 months postoperatively were within normal limits, with jitter of 0.74% and shimmer of 0.29 dB. His maximum phonation time was 12 seconds for a sustained vowel, and his perceptual speaking voice quality was normal.

This report verifies the successful reinnervation of a denervated laryngeal muscle using the muscle-nerve-muscle neurotization technique. The EMG recordings from the reinnervated cricothyroid muscles demonstrated resting motor unit potentials. There was a significant recruitment of motor units on EMG with higher-pitched phonation. Selective reinnervation was further confirmed for patient 1 by recording a response from the reinnervated muscle with stimulation of the contralateral donor muscle. Although the EMG evidence confirms reinnervation, it does not measure contractile function of the reinnervated muscle, and we are unable to objectively compare contractile function of the normal vs reinnervated side. However, indirect evidence suggests that the reinnervated cricothyroid muscle was functional. In all patients, the speaking voice was perceptually normal, and jitter and shimmer were within normal limits. All patients had a wide frequency range of their voices and were able to perform high-pitch tasks without significant pitch breaks. We speculate that their better voice quality and their enhanced ability to control voice pitch without significant breaks are related to the reinnervation and functional recovery of the previously denervated cricothyroid muscle. This allows the patients to symmetrically increase the tension in both TVFs, resulting in better control over voice pitch. Crumley and Izdebski described a patient with a high vagal lesion who had good voice quality after laryngeal innervation with ansa hypoglossi to RLN anastomosis. The patient was a singer and wanted a better voice quality and pitch control. The patient underwent a cricothyroid muscle reinnervation by direct suturing of the contralateral ansa hypoglossi to the denervated muscle. Postoperatively, an improvement in pitch control and production of the higher voice fundamental frequencies was noted within 4 months. Thus, with a nerve transfer operation that would primarily provide tone to the cricothyroid muscle, the vocal capabilities were believed to have been improved. We would expect that motion-specific reinnervation...
achieved through muscle-nerve-muscle neurotization would give even better voice quality due to active muscle control.

Muscle-nerve-muscle neurotization represents a novel but largely unsubstantiated method for the reinnervation of skeletal muscle. As previously described, muscle-nerve-muscle neurotization is a surgical procedure whereby one end of an autogenous nerve graft is placed in the belly of an innervated muscle, and the distal end of the nerve graft is placed in the belly of a target, denervated muscle. By selecting an appropriate muscle, this technique has the potential to provide motion-specific innervation. The only report of this method has been by Millesi et al. The work describes a series of 6 patients with long-standing, unilateral orbicularis oris paralysis. Sural nerve grafts were harvested and one end was implanted in the innervated orbicularis oris muscle. The nerve grafts were then tunneled across the midline and the other end implanted in the denervated orbicularis oris. Sufficient reinnervation to restore oral competence and spontaneous, bilateral animation was obtained in all patients. Stimulation of the normal muscle elicited an evoked EMG response in the contralateral muscle, and a nerve biopsy specimen from one patient demonstrated multiple, myelinated axons within the nerve graft.

Theoretically, this technique for laryngeal reinnervation has many advantages. First, it can provide motion-specific reinnervation. There is considerable evidence demonstrating that reinnervated muscle takes on the characteristics of the donor nerve. Reinnervation of a muscle through nerve fibers routed from its contralateral equivalent should maintain the muscle’s fiber composition and its response and biochemical characteristics, which should result in optimal functional recovery. In addition, the reinnervated muscle should respond almost synchronously with the normally innervated contralateral muscle, resulting in near-normal coordination of laryngeal muscular functions. Second, the paired nature and proximity of laryngeal muscles make them ideal candidates for muscle-nerve-muscle reinnervation, and their relatively small size makes it likely that functional contractility can be achieved. The functional properties of laryngeal muscles reinnervated using this technique are currently being evaluated in an animal model.

In conclusion, the muscle-nerve-muscle neurotization technique was successful in providing selective reinnervation of the cricothyroid muscle in our 3 patients. This method has great potential for clinical application in cases of unilateral laryngeal paralysis.

Accepted for publication June 11, 2001.


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