Original Investigation

Laryngeal Electromyography-Guided Hyaluronic Acid Vocal Fold Injection for Unilateral Vocal Fold Paralysis
A Prospective Long-term Follow-up Outcome Report

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IMPORTANCE Unilateral vocal fold paralysis (UVFP) is a common voice disorder that may cause glottal closure insufficiency with hoarseness of voice. Laryngeal electromyography (LEMG)-guided hyaluronic acid vocal fold (VF) injection has been proposed as a treatment option to improve glottal closure with a satisfactory short-term effect. To our knowledge, this study reports the first long-term follow-up result of this treatment modality.

OBJECTIVE To present the long-term treatment results of LEMG-guided hyaluronic acid VF injection for UVFP.

DESIGN, SETTING, AND PARTICIPANTS Prospective study of the treatment results of 74 patients who received LEMG-guided hyaluronic acid VF injection for UVFP at a tertiary referral medical center from March 2010 to February 2013.

INTERVENTIONS In the office-based procedure, 1.0 mL of hyaluronic acid was injected via a 26-gauge monopolar injectable needle electrode into paralyzed thyroarytenoid muscles by LEMG guidance.

MAIN OUTCOMES AND MEASURES Various glottal closure evaluations such as normalized glottal gap area, maximal phonation time, phonation quotient, mean airflow rate, perceptual GRBAS (grade, roughness, breathiness, asthenia, strain) scale, and Voice Handicap Index were compared before and after injection using the nonparametric Wilcoxon signed rank test within 1 month, at 6 months, and at the last follow-up examination.

RESULTS Sixty patients had been followed up for at least 6 months. Forty-four patients received only 1 injection, and 16 patients received repeated injections (2 injections for 13 patients and 3 for 3 patients). All the glottal closure parameters improved significantly ($P < .001$) within 1 month, at 6 months, and at the last follow-up examination, with a mean (SD) of 17.4 (8.9) months. At the last follow-up examination, the mean (SD) normalized glottal gap area was significantly reduced from 7.9 (5.7) to 0.6 (1.6). Mean (SD) maximal phonation time was significantly prolonged from 4.6 (3.8) seconds to 12.1 (7.4) seconds. Mean (SD) phonation quotient was significantly reduced from 647 (508) mL/s to 277 (212) mL/s. Mean (SD) airflow rate was significantly reduced from 445 (338) mL/s to 175 (145) mL/s. When all the GRBAS scale parameters improved, the mean (SD) Voice Handicap Index score was significantly reduced from 76 (22) to 38 (30) (all $P < .001$).

CONCLUSIONS AND RELEVANCE Of the 74 patients in this study, 44 (60%) who received a single injection and 16 (22%) who received repeated injections did not require another treatment after long-term follow-up. Laryngeal electromyography-guided hyaluronic acid VF injection is an option for treating UVFP with satisfactory results.

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Incomplete vocal fold (VF) adduction in unilateral VF paralysis (UVFP) is a common disorder that may cause glottal closure insufficiency (GCI) with hoarseness of voice and aspiration during swallowing. In addition to laryngeal reinnervation, the surgical management of GCI includes open laryngeal framework surgery (medialization laryngoplasty) and VF injection to displace the paralyzed VF medially toward the midline and then improve the glottal closure during phonation.[1] Compared with open laryngeal framework surgery, VF injection is relatively noninvasive without a cervical open approach and can be done in the office setting. Since Bruening[2] started using VF injection to treat GCI of UVFP in 1911, it has become a popular treatment with various injectable materials including hyaluronic acid.[3] In the past, VF injection was always guided by laryngoscopy with different techniques.[4]

Laryngeal electromyography (LEMG) was introduced in 1944 by Weddel et al,[5] and it is the only test that can provide otolaryngologists with the neuromuscular status of patients with UVFP. In our previous study, the LEMG signal obtained from the thyroarytenoid muscle in a paralyzed VF provided 87.1% accuracy in predicting prognosis of UVFP.[6] In 1988, Ludlow et al[7] reported using LEMG to guide botulinum toxin injection into the thyroarytenoid muscle to relieve VF spasm in adductor spasmodic dysphonia. Because the thyroarytenoid muscle is the target of both LEMG and VF injection, we have prospectively investigated the therapeutic application of LEMG in patients with UVFP since 2010. In our preliminary reports, we have proved that LEMG-guided hyaluronic acid VF injection is a feasible office-based technique with satisfactory short-term results.[8] Besides, the obtained LEMG data may be helpful for future clinical strategy management of patients with UVFP, and this technique can be an optional initial management of UVFP.[9] In this prospective study, we evaluated the long-term treatment outcome of LEMG-guided hyaluronic acid VF injection for UVFP.

Methods

The present study was approved by the institutional review board of Taichung Veterans General Hospital, Taichung City, Taiwan, and all patients provided written informed consent for participation in the study. From March 2010 to Feb 2013, 74 consecutive patients with UVFP due to various causes visited our voice clinic for their hoarseness and proneness to choking with varying degrees of severity. Their UVFP and GCI were confirmed and recorded by videostroboscopy. The digitized stroboscopic image of the larynx at the maximum closure during VF vibration was captured for analysis. The normalized glottal gap area (glottal gap area [pixels × pixels]/the square of unaffected side membrane VF length [pixels × pixels] × 100, as defined by Omori et al[10]) was measured by computer software (Image J, 1.42q, Wayne Rasband, National Institutes of Health) to quantify the glottal gap.

As is routine in the management of voice disorders, each patient's habitual comfortable voice was audiotaped, and several aerodynamic parameters including maximal phonation time, phonation quotient, and mean airflow rate under comfortable phonation were recorded by a commercially available system (Aerophone II; Kay Elemetrics Corp) in the voice laboratory. According to the GRBAS (grade, roughness, breathiness, asthenia, strain) system developed by the Japanese Society of Logopedics and Phoniatrics,[11] our speech pathologist (H.-C.L.) performed perceptual evaluation of patients' voice quality. The Voice Handicap Index (VHI) questionnaire, developed by Jacobson et al,[12] was scored by patients to grade the severity of their voice handicap. The aforementioned laryngeal function analysis parameters are summarized in eTable 1 in the Supplement. All the parameters were recorded before and after the injection during follow-up.

All patients received LEMG for evaluation of the neuromuscular function of immobile VF and guidance of hyaluronic acid injection, which was described in detail in our previous publications.[6,8,9] Briefly, after patients were placed in a supine position without using any anesthesia, the first author (C.-C.W.) inserted a 26-gauge monopolar injectable needle electrode (Bo-ject Disposable Needle Electrode, AlpineBiomed ApS) at the level of the cricothyroid membrane on the normal side of the larynx approximately 0.5 cm from the midline. The needle was angled superiorly 30° to 45° with an approximate depth of 1 to 2 cm to approach the thyroarytenoid muscle. The patient was asked to repeat a sustained vowel /i/ to confirm the position of the needle and that the LEMG was working properly on the normal side of the thyroarytenoid muscle. We repeated the puncture at the paralyzed side thereafter, and the second author (M.-H.C.) interpreted the signal of the paralyzed thyroarytenoid muscle. The preset rule first proposed by Munin et al[13] and verified by our previous study[6] was used to predict the prognosis of UVFP. Normal or nearly normal motor unit recruitment and absence of spontaneous activities such as fibrillations or positive sharp waves determine a good prognosis; otherwise, the prognosis is considered poor. After completion of signal recording, 1.0 mL of hyaluronic acid Restylane Perlane (Q-Med) was injected via the 26-gauge needle into the thyroarytenoid muscle to augment the paralyzed VF (eFigure 1 in the Supplement and **Video 1**).

After hyaluronic acid injection, the data for the aforementioned laryngeal function parameters were collected again within 1 month, then every 3 months during the first-year follow-up and every 6 months during the second-year follow-up. When patients experienced diminishment of the injection effects due to hyaluronic acid absorption, they could choose repeated injection or permanent laryngeal framework surgery if the LEMG showed poor prognosis. If patients had long-term injection benefit, they maintained follow-up for observation of VF function recovery. The data of parameters collected before injection, within 1 month after injection, 6 months after injection, and at the last follow-up examination were analyzed with the nonparametric Wilcoxon signed rank test by using SPSS software, version 10.0.7 (SPSS Inc). Statistical significance was defined as $P < .05$.

Results

Seventy-four patients (31 male and 43 female) were recruited for study, and their ages ranged from 20 to 84 years with a mean of 52.0 years. For our 74 patients, all injections were per-

Table 1. The Long-term Follow-up Results of the 60 Patients After Injection

Parameter	Injection, Mean (SD)			At 6 mo, Mean (SD)		At Last Follow-up, Mean (SD)	
	Before	After	*P* Value		*P* Value		*P* Value
NGGA[a]	7.9 (5.7)	0.4 (0.8)	<.001	0.9 (1.9)	<.001	0.6 (1.6)	<.001
MPT, s	4.6 (3.8)	10.2 (5.8)	<.001	11.3 (6.5)	<.001	12.1 (7.4)	<.001
PQ, mL/s	647 (508)	321 (247)	<.001	275 (185)	<.001	277 (212)	<.001
MAFR, mL/s	445 (338)	183 (180)	<.001	176 (135)	<.001	175 (145)	<.001
GRBAS scale[b]							
Perceptual G	2.0 (0.8)	0.7 (0.7)	<.001	0.5 (0.7)	<.001	0.6 (0.8)	<.001
Perceptual R	1.3 (0.8)	0.5 (0.6)	<.001	0.4 (0.6)	<.001	0.5 (0.6)	<.001
Perceptual B	1.8 (0.8)	0.5 (0.7)	<.001	0.3 (0.7)	<.001	0.3 (0.7)	<.001
Perceptual A	1.9 (0.9)	0.4 (0.7)	<.001	0.5 (0.6)	<.001	0.5 (0.7)	<.001
Perceptual S	1.1 (0.7)	0.5 (0.6)	<.001	0.4 (0.6)	<.001	0.4 (0.6)	<.001
VHI[c]	76 (22)	39 (23)	<.001	37 (29)	<.001	38 (30)	<.001

Abbreviations: GRBAS, grade, roughness, breathiness, asthenia, strain; MAFR, mean airflow rate; MPT, maximal phonation time; NGGA, normalized glottal gap area; PQ, phonation quotient; VHI, Voice Handicap Index.

[a] Glottal gap area (pixels × pixels)/the square of unaffected side membrane vocal fold length (pixels × pixels) × 100.

[b] GRBAS scale score range for each parameter: 0 to 3 (0, normal; 1, slight; 2, moderate; and 3, severe).

[c] VHI score range: 0 to 120.

formed successfully at our clinic in 10 to 20 minutes without anesthesia or sedation. Because the injection was done via 26-gauge fine needles and the pain was tolerable, no injection was terminated during the procedure and no complications were noted thereafter.

During follow-up, 14 patients dropped out of the study. Of those 14 patients, 2 died of malignant disease, 2 received other VF surgical procedures, and 10 did not fulfill the requirement of at least 6 months' follow-up, so their data were excluded from analysis. The other 60 patients were followed up for more than 6 months unless they recovered VF function within 6 months after injection. The mean (SD) follow-up duration was 17.4 (8.9) months. Forty-four patients had only 1 injection with a mean (SD) follow-up of 16.2 (8.9) months. Sixteen patients had repeated injections (2 injections for 13 patients and 3 for 3 patients) with a mean (SD) follow-up of 20.7 (8.1) months (eFigure 2 in the Supplement). Immediately after injection within the 1-month follow-up for the 60 patients, all parameters, including normalized glottal gap area, maximal phonation time, phonation quotient, and mean airflow rate, perceptual GRBAS scale, and VHI, significantly improved ($P < .001$) after the injection (**Table 1**). The results again confirmed the effectiveness immediately after the injection. Regarding the long-term result, the measured parameters 6 months after injection and at the last follow-up examination for the included 60 patients are also summarized in Table 1. According to the results, all the evaluation parameters significantly improved.

In addition, we also separately analyze the data of the single-injection group (44 patients) and the repeated-injection group (16 patients). In the single-injection group, the follow-up duration ranged from 6 months (recovered VF motion within 6 months) to 45 months with a mean (SD) of 16.2 (8.9) months. According to the results (**Table 2**), all parameters at the 6-month and last follow-up examination for the single-injection group significantly improved. The long-term benefit of a patient is presented in **Figure 1**.

In the repeated-injection group, all parameters within 1 month after injection also improved significantly ($P < .001$). Thirteen patients received 2 injections. After excluding 1 outlier, the first injection was given at a mean (SD) of 3.7 (1.9) months; the second injection was given at 7.9 (6.8) months, and the last follow-up examination was at 20.7 (8.1) months after the onset of symptoms. In the 3 patients who received 3 injections, the first injection was given at a mean (SD) of 3.5 (2.1) months, the second injection was given at 4.0 (2.4) months, the third injection was given at 12.0 (6.5) months, and the last follow-up examination was at 28.0 (7.1) months after the onset of symptoms. In the repeated-injection group, all of the aforementioned parameters remained significantly improved at the last follow-up examination except the perceptual strain scale (Table 2). Although the perceptual strain score did not reach statistical significant reduction at the last follow-up examination, the mean value was still reduced after the treatment and the VHI score that reflects quality of life was significantly improved.

During our long-term follow-up of the 60 patients, 5 patients in the single-injection group and 1 patient in the repeated-injection group recovered VF motion (**Figure 2**). Of the 6 patients who recovered VF motion, 3 had a good prognosis according to the first LEMG result; 1 patient received a second injection and the other 2 patients received a single injection before the recovery. In our long-term follow-up, no patients experienced long-term injection complications such as VF granuloma formation or voice deterioration.

Discussion

One of the mainstays of surgical treatment of UVFP is the concept of medialization, in which the paralyzed VF is displaced toward the midline to facilitate glottal closure. In addition to medialization laryngoplasty, VF injection has been com-

Table 2. The Long-term Follow-up Results of the 44 Patients Who Received Only 1 Injection and the 16 Patients Who Received Repeated Injections

Parameter	Mean (SD)		P Value	At Last Follow-up, Mean (SD)	P Value
	Before Injection	At 6 mo			
1 Injection (n = 44)					
NGGA[a]	8.1 (6.4)	0.6 (1.5)	<.001	0.4 (1.2)	<.001
MPT, s	5.0 (4.3)	12.2 (6.9)	<.001	13.8 (7.7)	<.001
PQ, mL/s	658 (546)	264 (189)	<.001	232 (185)	<.001
MAFR, mL/s	453 (368)	166 (127)	<.001	146 (133)	<.001
GRBAS scale[b]					
Perceptual G	2.0 (0.8)	0.4 (0.6)	<.001	0.4 (0.7)	<.001
Perceptual R	1.2 (0.8)	0.4 (0.5)	<.001	0.4 (0.5)	<.001
Perceptual B	1.6 (0.7)	0.2 (0.6)	<.001	0.3 (0.6)	<.001
Perceptual A	1.9 (0.8)	0.4 (0.6)	<.001	0.2 (0.6)	<.001
Perceptual S	1.1 (0.7)	0.2 (0.4)	<.001	0.2 (0.5)	<.001
VHI[c]	71 (21)	33 (28)	<.001	31 (30)	<.001
Repeated Injections (n = 16)					
NGGA[a]	7.3 (3.4)	1.8 (2.6)	<.001	1.1 (2.4)	<.001
MPT, s	3.6 (1.9)	8.4 (4.1)	<.001	7.3 (3.4)	<.001
PQ, mL/s	615 (39)	310 (174)	.008	398 (239)	.02
MAFR, mL/s	425 (245)	207 (157)	.001	254 (151)	.007
GRBAS scale[b]					
Perceptual G	2.1 (0.7)	0.8 (0.9)	<.001	1.1 (0.9)	.002
Perceptual R	1.5 (0.7)	0.6 (0.7)	<.001	0.7 (0.8)	.003
Perceptual B	2.1 (0.8)	0.6 (0.7)	<.001	0.9 (0.7)	<.001
Perceptual A	1.8 (0.9)	0.8 (0.7)	.001	0.6 (0.9)	.006
Perceptual S	1.3 (0.6)	0.7 (0.8)	.01	0.8 (0.9)	.07
VHI[c]	87 (19)	50 (28)	.001	55 (27)	.001

Abbreviations: MAFR, mean airflow rate; MPT, maximal phonation time; NGGA, normalized glottal gap area; PQ, phonation quotient; VHI, Voice Handicap Index.

[a] Glottal gap area (pixels × pixels)/the square of unaffected side membrane vocal fold length (pixels × pixels) × 100.

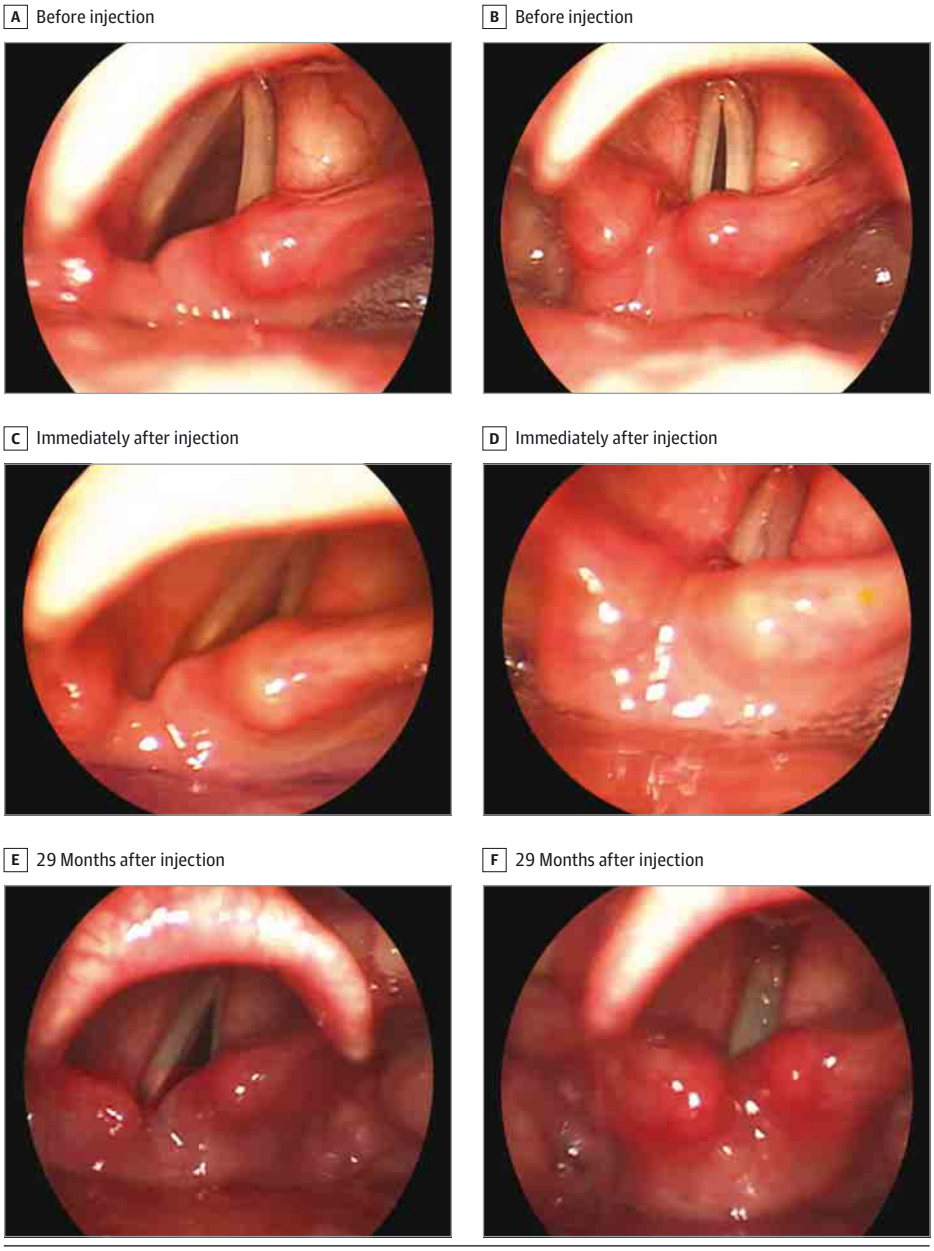
[b] GRBAS scale score range for each parameter: 0 to 3 (0, normal; 1, slight; 2, moderate; and 3, severe).

[c] VHI score range: 0 to 120.

monly used for medialization since 1911.[2] Recently, Sulica et al[4] reviewed the current practices in VF injection techniques. They found that office-based awake VF injection was rapidly adopted over the past 5 years in the United States because of its clinical utility, low complication rate, and cost and time advantages. In their review, they categorized awake VF injection techniques as peroral, transthyrohyoid, and transthyroid cartilage injections and transcricothyroid injections and noted that the transcricothyroid approach is the technique used most often (47%). All of the aforementioned techniques are performed using flexible laryngoscope guidance. In 2012, we published the first article that proved LEMG could be used to guide transcervical transcricothyroid hyaluronic acid VF injection, and the short-term results were satisfactory.[8] The rationales for our technique have been clearly described in our previous article.[8]

According to our results, the effect of office-based LEMG-guided hyaluronic acid VF injection for UVFP is variable. However, of our 74 patients, 44 (59%) did not require further treatment at a mean (SD) of 16.2 (8.9) months after a single injection. In the literature, Hertegård et al[14] reported 60% of their patients had long-term benefit after hyaluronic acid injection. Carroll and Rosen[15] reported long-term effect at a mean of 18.6 months in 22 patients after calcium hydroxylapatite injection. Thus, our long-term result is similar to those 2 pioneer laryngeal injection studies. There are 3 main rationales for an absorbable hyaluronic acid injection to have a long-term augmentation effect on patients with UVFP. First, Restylane Perlane, one of the hyaluronic acid products of the Restylane family used in our study, is a nonanimal stabilized hyaluronic acid gel that is produced biotechnologically by bacterial fermentation. It undergoes isovolemic degradation by which it aggregates more water as it is absorbed; hence, it can maintain the volume in the injection area for a longer period than an autologous transplant.[16] An animal study showed that commercial hyaluronic acid can also stimulate the injected VF to regenerate some connective tissues including collagen and endogenous hyaluronic acid.[17] Therefore, some patients could have a longer lasting effect while the absorbed hyaluronic acid volume was replaced by water or endogenous soft tissue. Second, in another animal study, Woodson[18] confirmed that there is a strong propensity for laryngeal reinnervation after recurrent laryngeal nerve injury and VF paralysis. Preferential reinnervation of paralyzed adductor muscles may account for a medial position of the paralyzed VF. The atrophic thyroarytenoid muscle could also regain some muscle bulk after the regeneration.[18] Third, spontaneous gradual recovery of voice may occur in the absence of VF motion in some patients with UVFP. This type of recovery is thought to result from adaptation of the intact VF, thereby allowing for laryngeal compensation and effective glottic closure without actual reanimation of the paralyzed VF.[19] During the gradual absorption of injected hyaluronic acid in some of our patients, the contralateral healthy VF probably compensated for the glottis clo-

Figure 1. Stroboscopic Findings Before and After Injection in a Patient With Unilateral Vocal Fold Paralysis and Poor Prognosis

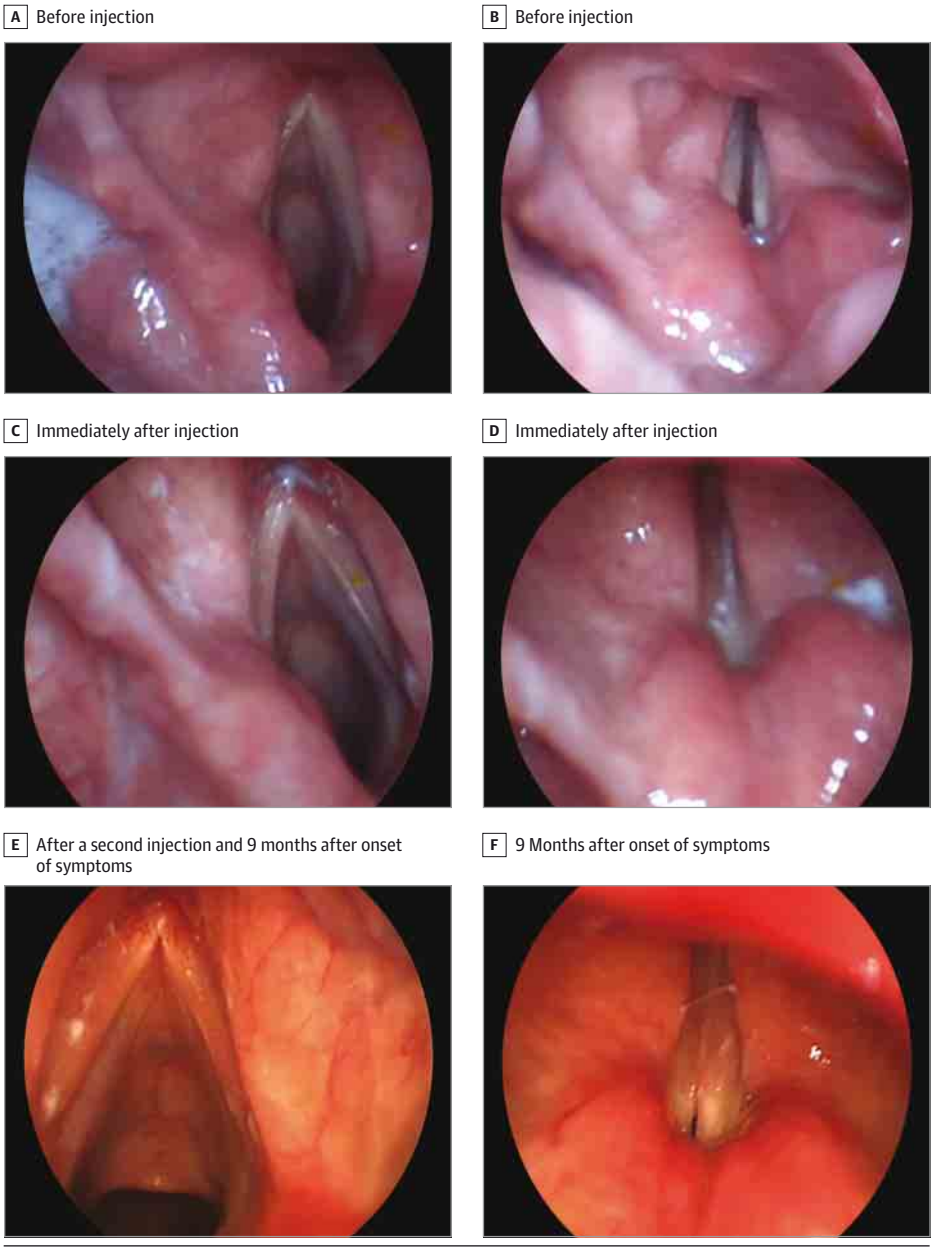


A, Before injection, the patient's right vocal fold was immobile without abduction during inspiration. B, Before injection, the patient had a constant glottal gap between the membranous portions of the bilateral vocal folds during phonation. C, Immediately after injection, the right vocal fold was augmented and medialized to the midline. D, Immediately after injection, the patient's glottis could close during phonation. E, Twenty-nine months after injection, the patient's right vocal fold was still immobile without abduction during inspiration. F, Twenty-nine months after injection, the patient's glottis still closed perfectly during phonation owing to a persistent augmentation effect.

sure. The aforementioned 3 hypotheses account for the long-term benefit in more than half of our patients.

From the study of Sulica et al[4] we know that otolaryngologists continue to use a variety of techniques and materials to treat GCI because each technique has its pros and cons. They noted that the choice of injection technique is usually based on surgeon preference. Each surgeon tended to adopt one particular method after initial trials of multiple techniques, reserving other techniques for unusual circumstances or to salvage technical failures. Our technique also has some advantages, and hopefully it will become a new option of treatments for other surgeons. For example, anesthesia could be spared in our technique. Because a thin, 26-gauge LEMG injectable needle electrode was used, the transcervical injection pain was tolerable in all our injections. Especially for patients without a prominent laryngeal cartilage, subcutaneous anesthesia might obscure the cricothyroid notch and hinder the surgeon from locating the transcricothyroid puncture site. Besides, topical anesthesia to laryngeal mucosa that is used in peroral or transthyrohyoid VF injection could overanesthetize the larynx and cause salivary secretions to overwhelm the larynx, making the patient uncomfortable and obscuring the image guidance during injection.[4] However, underanesthetization could also be a problem. In the study by Sulica et al,[4] patient discomfort accounted for the largest number of awake injection failures. They suggested that a strong gag reflex that

Figure 2. Stroboscopic Findings Before and After Injection in a Patient With Unilateral Vocal Fold Paralysis and Good Prognosis



A, Before injection, the patient's left vocal fold was immobile without abduction during inspiration. B, Before injection, the patient had a constant glottal gap between the membranous portions of the bilateral vocal folds during phonation. C, Immediately after injection, the left vocal fold was augmented and medialized to the midline. D, Immediately after injection, the patient's glottis could close during phonation. E, After a second injection and 9 months after the onset of symptoms, the patient's left vocal fold motion was restored and bilateral vocal folds could achieve symmetrical full abduction during inspiration. F, Nine months after the onset of symptoms, the patient's glottis could close perfectly after the recovery of left vocal fold motion.

persists through topical anesthesia is generally a contraindication for awake injection. Compared with the scope-guided techniques used by Sulica et al,[4] our LEMG-guided hyaluronic acid VF injection avoids the flexible laryngoscope or transoral VF mucosa puncture that could irritate the mucosa of the upper airway and induce a cough or gag reflex. Actually, all of our patients successfully underwent the procedure without any anesthesia. It seems that our technique could be ideal for patients with aforementioned anesthesia issue, strong gag, or severe cough reflex.

The most significant feature of our technique is sparing the laryngoscopic guidance. In addition to the aforementioned anesthetization issue, several other factors often hinder laryngoscope-guided injection from success. For example, in the most commonly used transcricothyroid injection, Sulica et al[4] reminded us that the location of the needle cannot be directly seen. We can only estimate the position of the needle by identification of transmitted motion within the VF, which sometimes proves to be difficult. For patients who are not good candidates for laryngoscopic guidance injection under local anesthesia, our technique provides an alternative solution. Although we did not have visual guidance by laryngoscope, the LEMG helped us to locate the thyroarytenoid muscle. This kind of deep muscle injection is important to prevent the complications caused by superficial injection into the submucosa, ie,

Reinke space, of the VF. In the report by Gillespie et al,[20] complications of superficial injection of calcium hydroxylapatite occurred in 5 of 39 patients (13%).

In our approach, the major role of LEMG is to guide the injection similar to the way botulinum toxin injection is guided for spasmodic dysphonia. In most procedures, the fibrillation or reduced recruitment signal could be used easily to locate the paralyzed thyroarytenoid muscle. In rare cases of a patient with near electrical silence, it is also possible to successfully augment the paralyzed VF (**Video 2**). In our experience, when we falsely punctured the needle tip into the airway during patient's phonation of /i/, the speaker broadcasted the patient's voice louder and it sounded like the patient was using a microphone. In addition the LEMG also revealed regular waves that were significantly different from the motor unit potentials. If we confirmed that the needle tip was between the airway and thyroid cartilage, a nearly silent electrical signal could also be used to locate the paralyzed thyroarytenoid muscle. The other valuable characteristic of our technique is that the prognosis of UVFP can be obtained simultaneously during the procedure. The additional LEMG data will benefit future clinical consultation or research on LEMG. According to our previous retrospective study, the accuracy of LEMG in predicting the outcome of UVFP is 87.1%.[6] However, the hyaluronic acid injection cannot guarantee a permanent effect. If a patient's symptoms recur after the injection, a poor prognosis will be clinical evidence that the patient should undergo permanent open laryngeal framework surgery. Contrarily, a good prognosis following LEMG may encourage patients to receive repeated injections and then wait for recovery. The benefit of this strategy has been clearly described in our preliminary report,[8] Briefly, the LEMG information is for guidance and has the occasional secondary benefit of some prognosis[9] (eTable 2 in the Supplement).

In addition to the 44 patients with long-term benefit after a single injection, approximately one-fifth (16of 74 patients) maintained long-term benefit after the second or third injection. According to the literature, recent data suggest that early VF injection medialization may be significantly associated with a lower rate of eventual need for permanent open medialization laryngoplasty.[21,22] However, further studies will be needed to confirm this finding. It will be the objective of our future research. Besides, readers may concern about the borderline improvement (P = .07) for perceptual strain scale in the repeated injection cohort at final follow-up (Table 2). Theoretically, the most significant perceptual character of UVFP voice is breathiness induced by GCI. The perceptual strain was only noted in some of this cohort caused by compensatory supraglottic hyperfunction,[23] and the relatively small number of repeated injection cohort might be the reason of insignificant improvement in strain. Anyway, all other parameters and VHI reflecting the quality of life still achieved significant improvement.

Our study has several limitations. First of all, surgeons need to be familiar with performing LEMG. However, it is not a difficult technique for most laryngologists. Since it was developed in 1944, LEMG has been widely used for guiding botulinum toxin injection for spasmodic dysphonia and predicting the prognosis of UVFP.[6,7,24] In addition, an electromyographic machine is not a common piece of equipment in an otolaryngological department, which may also be a drawback. However, a voice surgeon could cooperate with neurologist to compensate for this inconvenience. Second, our LEMG-guided injection technique only proves the safety of hyaluronic acid injection. Because hyaluronic acid is highly biocompatible with VF tissue, it has been proved to be safe not only in deep muscle injection but also in superficial injection.[25] Chan and Titze[26] suggested that hyaluronic acid may be a potentially optimal bioimplant for VF mucosal defects and lamina propria deficiencies from a biomechanical standpoint. Thibeault et al[27] also discovered that hyaluronic acid possesses unique properties in improving either tissue composition or biomechanical properties of injured VFs. Our long-term study results without complications further indicate that LEMG-guided VF injection is safe when hyaluronic acid is used as an augmentation material. Third, readers might be concerned about the imprecision of injection without laryngoscopy guidance or uniformity of injecting 1 mL of hyaluronic acid in all patients. This issue has been clearly addressed in our preliminary report.[8] To be brief, 1 mL of hyaluronic acid is larger than the mean volumes of VF injection material used in the study by Carroll with Rosen[15] and Hertegard et al[28]; therefore, a 1-mL injection was usually enough to achieve overcorrection of a paralyzed VF. Because VF overinjection is common with absorbable material and the shape of the overinjected VF will be remodeled in response to the compression from the contralateral mobile VF, delicate visual monitoring of the hyaluronic acid injection amount and injection site by laryngoscopy will become less important.[8] However, surgeons need to confirm that the contralateral healthy VF can fully abduct before the injection, but this precaution is mandatory for any VF medialization procedures. Clinically, if contralateral VF motion is normal, visual monitoring of the airway is not important even if the paralyzed VF could be overinjected. That is why a paralyzed VF is usually overinjected with autologous fat graft under general anesthesia.[29]

Conclusions

Laryngeal electromyography-guided hyaluronic acid VF injection is a feasible and safe initial management strategy for UVFP. No complications were found in our long-term follow-up period. The duration of injection augmentation effect varies. However, most of our patients (59%) did not require another treatment after long-term follow-up after a single injection. When the effect of VF injection diminishes, the prognostic information obtained from LEMG can be used as guidance for future open laryngeal framework surgery. Because the procedure is simple and well tolerated, some of our patients with a poor prognosis preferred repeated injections to maintain their voice quality in the long term.

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