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Additional Injection Laryngoplasty for Patients With Unilateral Vocal Fold Paralysis

Nayeon Choi, MD ☞; Seongjun Won, MD; Hokyung Jin, MD; Hack Jung Kim, MD; Woori Park, MD; Young-Ik Son, MD, PhD ☞

INTRODUCTION

Injection laryngoplasty (IL) became a major treatment option for a variety of vocal fold disorders because of its less invasiveness and development of biocompatible injection materials.1,2 Recently, IL is preferred to other invasive procedures including arytenoid adduction and medialization thyroplasty, since IL provides similar subjective and objective voice outcomes with better cost-effectiveness in comparison to open laryngeal framework surgeries.3,4

With IL, the voices of patients with unilateral vocal fold paralysis (UVFP) may improve by vocal fold augmentation with biocompatible material and/or compensation of vocal fold movement.2,5 However, the absorption rate of the injection material and the degree of compensation varies from patient to patient, therefore it is not easy to precisely predict postprocedural voice outcomes.6 In case of insufficient augmentation of vocal fold, additional procedures including additional IL or laryngeal framework surgery can be the next options of treatment.7 However, many patients are reluctant to receive open voice surgery, which will result in surgical neck scar and discomfort during the recovery period. Therefore, additional IL is preferred in most of the patients who had unsatisfactory voice outcomes after initial IL. A few previous reports described about the patients with multiple IL, but they did not evaluate the subjective and objective voice outcome of additional IL in comparison with initial IL.7,8

In this study, we performed additional IL in UVFP patients who had insufficient vocal fold augmentation and unsatisfactory voice outcome despite the initial IL. We evaluated objective and subjective voice parameters before and after each IL, and compared voice outcomes of additional IL to those of initial IL.

MATERIALS AND METHODS

Patients

This study was approved by Samsung Medical Center Institutional Review Board (Approval No. 2018-08-062). The patients who received IL between 2006 and 2016 at the authors’ institution were reviewed. Total 629 patients received IL during the study period, and 54 patients were excluded due to the lack of voice tests (Fig. 1). Four-hundreds sixty-five patients who received only one IL were not included in this study. Among the 105 patients who had additional

OBJECTIVES: In case of insufficient voice improvement after injection laryngoplasty (IL), additional IL will be one of the next option of treatments. However, little is known about the voice outcomes regarding an additional IL.

Study design: Retrospective comparative study in single institution.

Methods: We enrolled the patients of unilateral vocal fold paralysis (UVFP), who received IL (N = 76) twice because of insufficient voice improvement. The etiologies of UVFP were related with thoracic and esophageal surgery (51.3%), neck surgery (30.3%), skull base surgery (7.9%), or unknown (10.5%). The subjective and objective voice parameters were collected before and after (mean: 5.3 months) each IL.

Results: Aspiration, maximum phonation time (MPT), jitter percentage, shimmer percentage, and noise to harmonic ratio (NHR) were significantly improved after both the first and second rounds of IL (P < .001). Voice handicap index (VHI)-30 was also significantly improved after both the first and second rounds of IL (P < .001). Regarding GRBAS score, overall grade of dysphonia (G), roughness (R), and breathiness (B) were significantly improved after the first IL, but only G and R after the second IL (P < .05). In comparison between postprocedural voice parameters of the first and second ILs, MPT was significantly improved from 5.5 ± 3.5 seconds to 7.3 ± 7.5 seconds (P = .001). Grade of dysphonia (1.9 ± 0.8) and breathiness (1.7 ± 0.9) of post-first IL were significantly improved (P < .001) to those of post-second IL (1.3 ± 0.7 and 1.2 ± 0.7, respectively). VHI-30 of post-first IL (72.0 ± 20) was significantly improved (P < .001) to those of the second IL (57.2 ± 23.7).

Conclusions: In selected patients, additional IL could provide further improvement of voice in patient who had unsatisfactory voice results despite of initial IL.

Key Words: Vocal fold paralysis, multiple, additional, injection laryngoplasty.

Level of Evidence: 4

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intervention after initial IL, we finally evaluated 76 patients who received additional IL.

Among the patients who were not satisfied with their voice after initial IL, we selected appropriate candidates for additional IL. At first, we considered patients' preference for IL versus open laryngeal framework surgery. In addition, we considered patients' vocal demands including social and occupational needs within their environment related to noise. Finally, we recommended arytenoid adduction surgery for patients who had relatively large posterior glottal gap and/or vertical height discrepancy between two vocal folds during the /e/ phonation.

Injection Laryngoplasty Procedure

We performed IL through cricothyroid membrane approach under local anesthesia. Patients inhaled a 4% lidocaine using nebulizer for 5 minutes, and 2% lidocaine was injected at the subcutaneous layer around the cricothyroid membrane. Flexible fiberoptic nasopharyngoscope (VNL-1530T, Pentax, Tokyo, Japan) was introduced through the nostril to visualize the larynx. The cricothyroid membrane was palpated and 23-guage spinal needle was introduced into paralyzed vocal fold until the needle tip was bluntly seen at the anterolateral side of the vocal process of arytenoid cartilage. We used ArteSense (European Medical Contract Manufacturing B.V., Nijmegen, The Netherlands) composed of 80% volume of denatured bovine collagen and 20% of polymethyl methacrylate (PMMA) microspheres. In most cases, 0.5–0.7 ml of ArteSense was injected to make slight over-correction of the paralyzed vocal fold. The patients were observed for 2 hours after IL to check complications including allergic reaction, bleeding, and dyspnea.

Voice Analyses

When UVFP is noticed, we routinely searched for the possible reasons of paralysis by history taking and/or CT scans covering from skull base to mid-thorax. We also evaluated the presence of uvula deviation (soft palate paralysis) as well as saliva pooling at the pyriform sinus (pharyngeal paralysis) to localize the point of nerve paralysis.

The voice evaluation including subjective and objective voice parameters were performed before and 3 to 6 months (mean 5.3 months) after IL. As a part of voice evaluation, we asked patients about aspiration symptoms including cough, sputum, and fever. Modified barium swallowing test, chest x-ray and serum inflammatory index (CBC, CRP, ESR) were checked when significant aspiration was suspected. Voice therapy (education for vocal exercise and vocal hygiene) was provided by two experienced speech language pathologists along with voice evaluation.

Laryngeal stroboscopic evaluations (Pentax, Lincoln Park, NJ, USA) were performed at each follow-up visit. In addition to

### TABLE I.
Demographics of the Patients Who Had a Second Additional Injection Laryngoplasty (N = 76).

<table>
<thead>
<tr>
<th>Clinical Factors</th>
<th>Variables</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr, mean ± SD)</td>
<td>58.4 ± 14.0</td>
</tr>
<tr>
<td>Gender (M:F) (N, %)</td>
<td>52.24 (68.4: 31.6)</td>
</tr>
<tr>
<td>Cause of paralysis (N, %)</td>
<td>Thoracic and esophageal surgery 39 (51.3)</td>
</tr>
<tr>
<td></td>
<td>Neck surgery 23 (30.3)</td>
</tr>
<tr>
<td></td>
<td>Skull base surgery 6 (7.9)</td>
</tr>
<tr>
<td></td>
<td>Unknown 8 (10.5)</td>
</tr>
<tr>
<td>Time interval between first and second injection laryngoplasty (mo, mean ± SD, min-max)</td>
<td>8.1 ± 7.9 (1–52)</td>
</tr>
</tbody>
</table>
TABLE II.
Voice Outcomes Before and After Each Injection Laryngoplasty in Patients Who Underwent a Second Additional Injection Laryngoplasty.

<table>
<thead>
<tr>
<th></th>
<th>First Injection Laryngoplasty</th>
<th>Second Injection Laryngoplasty</th>
<th>Pre vs Post of First IL§</th>
<th>Pre vs Post of Second IL§</th>
<th>Post First vs Second IL§</th>
<th>△(Post-pre) First vs Second IL§</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspiration (N, %)</td>
<td>16 (21.1)</td>
<td>4 (5.3)</td>
<td>4 (5.3)</td>
<td>2 (2.6)</td>
<td>.001</td>
<td>.317</td>
</tr>
<tr>
<td>MPT (sec, mean ± SD)</td>
<td>4.5 ± 3.6</td>
<td>5.5 ± 3.5</td>
<td>5.4 ± 3.3</td>
<td>7.3 ± 7.5</td>
<td>&lt;.001</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Jitter (%)</td>
<td>5.6 ± 4.0</td>
<td>4.7 ± 4.7</td>
<td>4.6 ± 4.7</td>
<td>2.8 ± 2.4</td>
<td>.022</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Shimmer (%)</td>
<td>11.6 ± 7.3</td>
<td>9.0 ± 6.5</td>
<td>9.1 ± 6.4</td>
<td>7.3 ± 5.8</td>
<td>.002</td>
<td>.001</td>
</tr>
<tr>
<td>NHR (mean ± SD)</td>
<td>0.3 ± 0.2</td>
<td>0.2 ± 0.2</td>
<td>0.2 ± 0.2</td>
<td>0.2 ± 0.1</td>
<td>.039</td>
<td>.024</td>
</tr>
<tr>
<td>GRBAS scores (mean ± SD)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade of dysphonia</td>
<td>2.6 ± 0.7</td>
<td>1.9 ± 0.8</td>
<td>1.9 ± 0.8</td>
<td>1.3 ± 0.7</td>
<td>&lt;.001</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Roughness</td>
<td>0.6 ± 1.0</td>
<td>0.4 ± 0.7</td>
<td>0.5 ± 0.8</td>
<td>0.6 ± 0.8</td>
<td>.038</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Breathiness</td>
<td>2.5 ± 0.7</td>
<td>1.7 ± 0.9</td>
<td>1.8 ± 0.9</td>
<td>1.2 ± 0.7</td>
<td>&lt;.001</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Astenia</td>
<td>0.2 ± 0.6</td>
<td>0.1 ± 0.4</td>
<td>0.1 ± 0.3</td>
<td>0.1 ± 0.3</td>
<td>.145</td>
<td>.589</td>
</tr>
<tr>
<td>Strain</td>
<td>0.1 ± 0.3</td>
<td>0.1 ± 0.4</td>
<td>0.1 ± 0.4</td>
<td>0.1 ± 0.3</td>
<td>.915</td>
<td>1.000</td>
</tr>
<tr>
<td>VHI-30 (mean ± SD)</td>
<td>81.2 ± 20.3</td>
<td>72.0 ± 20.7</td>
<td>73.7 ± 19.0</td>
<td>57.2 ± 23.7</td>
<td>&lt;.001</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

Values written in bold indicate \( p \)-value under 0.05.

IL = injection laryngoplasty; MPT = maximum phonation time; NHR = noise to harmonic ratio; SD = standard deviation; VHI = voice handicap index.
△(Post-pre): difference between voice test results before and after each injection laryngoplasty.
*Pre vs post of first IL: comparison of voice parameters before and after first injection laryngoplasty.
†Pre vs post of second IL: comparison of voice parameters before and after second injection laryngoplasty.
‡Post first vs second IL: comparison of preprocedural voice parameters of first and second injection laryngoplasty.
§△(Post-pre) first vs second IL: comparison of variance between preprocedural and postprocedural voice parameters of first and second injection laryngoplasty.
other voice outcome results, stroboscopic findings (patterns of glottal closure, size of glottic gap, vertical level difference, vocal atrophy, and compensatory contraction of the supraglottic structures) were important references to decide the next treatment plan including voice therapy, injection laryngoplasty and/or laryngeal framework surgery.

MDVP (Multi-Dimensional Voice Program, Model 4500, Kay, NJ, USA) software was used for acoustic analysis. The patient was seated in a sound-proofed room and a head-worn microphone (AKG, C410, Vienna, Austria) was placed 3 cm from the patient’s mouth. The patient was asked to produce the vowel /a/ for 3 seconds at a comfortable pitch and loudness.

Phonation time was determined by measuring the waveform signal using MDVP. The patient was asked to produce /a/ as long as possible at constant pitch and loudness. Maximum phonation time (MPT) was defined as the longest possible phonation time in three reiterations of the test.

For perceptual analysis, two experienced (20 and 5 years, respectively) speech pathologists in voice assessment listened to the recorded sentences and scored GRBAS scale. They discussed to make consensus on the GRABS score. For speaking analysis, we used two sentences (41 syllables) of “Kaul (Autumn)” standard passage, which is a phonetically balanced Korean passage. The patient was asked to read the sentences at a comfortable pitch, loudness, and rate.

The patients replied to a validated Korean version of voice handicap index (VHI–30 which is a set of self-rating questionnaires including the subscales of the functional, physical, and emotional aspects of the voice impairment.

Statistical Analysis
Pre- and postprocedural voice parameters were compared by paired sample T-test at each IL. Postprocedural voice parameters of initial IL and additional IL were also compared by paired sample T-test. Variances of voice parameters between before and after each IL were compared by paired sample T-test. P-value <.05 was considered as statistically significant. Statistical analyses were performed using SPSS for Windows ver. 20.0 (SPSS Inc., Chicago, IL, USA).

RESULTS
Baseline Characteristics of the Enrolled Patients
The age at the time of vocal fold paralysis diagnosis were 58.4 ± 14.0 years. Gender distribution of male to female was 54:24 (68.4%:31.6%) (Table I). The etiologies of vocal fold paralysis were related with thoracic and esophageal surgery (51.3%), neck surgery (30.3%), skull-base surgery (7.9%), and unknown cause (10.5%). Time interval between the first and second IL was 8.1 ± 7.9 months (min–max: 1–52 months).

Preoperative and Postoperative Voice Parameters of Each IL
The values of subjective and objective voice parameters were described in Table II. Incidence of aspiration symptom (n = 16, 21.1%) was significantly decreased (P = .001) after the first IL (n = 4, 5.3%) and it was further decreased after the second IL (n = 2, 2.6%) without statistical significance (P = .317). Objective voice parameters including MPT, jitter, shimmer, and NHR were significantly improved by the first and second IL, respectively. In terms of perceptual voice analysis, grade of dysphonia (G), roughness (R) and breathiness (B) significantly improved after the first IL. In contrast, GdBs significantly improved after the second IL. The subjective voice parameter VHI-30 improved significantly after each IL (P < .001).

Comparison of Postprocedural Voice Outcomes of First and Second IL
Voice outcomes after the first and second IL were compared to identify the effect of the second injection (Table II). Aspiration symptom was decreased from 5.3% (n = 4) to 2.6% (n = 2) of enrolled patients. MPT, jitter, and shimmer were significantly decreased after the second IL, but NHR was not improved despite of an additional IL (P = .051). Regarding GRBAS scores, G and B were significantly improved, but others were not. VHI-30 was significantly improved after the second IL.

The results of serial voice tests were demonstrated at Fig. 2. MPT, jitter, shimmer, and G improved after the first and second IL compared to those of before each IL. VHI-30 also improved after the first IL and improved further after the second IL.
Comparison of Variance Between Pre- and Post-IL

The amount of improvement in voice parameters after IL (△voice parameter) was calculated by subtracting voice test results before the injection from those after injection. Variances of voice parameters were compared to identify the degree of voice improvement after the first and second IL. Variance of MPT, jitter, shimmer, and NHR were not significantly different between the first and second IL. GRBAS scores also showed no significant differences. However, △VHI-30 of the second IL (−16.6 ± 19.4) was significantly greater (P = .003) in comparison with that of the first IL (−9.2 ± 21.3).

DISCUSSION

Recently, IL became the first-line treatment because of its non-invasiveness, ease of procedure, and development of biocompatible materials. Voice therapy including hard glottal attack, half swallow boom, abdominal breathing and head and neck relaxation is usually accompanied by surgical intervention. Voice therapy alone could be the treatment option for UVFP patients, but voice therapy together with surgical options is recommended. However, IL does not warrant satisfactory voice improvement because of unexpected absorption of injection material, insufficient vocal fold augmentation, and medialization. In the case of unsatisfactory results after IL, the next surgical options would be additional IL, arytenoid addition or medialization thyroplasty. However, little is known about the effects of these additional procedures after unsatisfactory initial IL.

In a previous report regarding additional procedures after IL with micronized dermis, 39% of patients underwent open laryngeal framework surgeries and 28% of patients received repeated IL. In another study of IL with fat tissues, 13.6% of the patients repeated multiple fat IL. However, these studies did not present the objective voice parameters after additional procedures and did not compare the voice outcomes between initial IL and additional procedures. In this study, we provided perceptual, acoustic, aerodynamic, and subjective voice parameters and compared voice outcomes between initial and additional IL. Most of voice parameters (grade of dysphonia, MPT, jitter, shimmer, NHR, and VHI-30) significantly improved following both of the first and second IL. Interestingly, amount of subjective voice improvement was significantly greater with the second IL, which means patients’ voice-related quality of life improved to a considerable degree by repeated IL in our study populations.

In this study, 76 (12.2%) of total 623 patients received the second IL, 13 (2.1%) had medialization thyroplasty, and 16 (2.6%) had arytenoid adduction as additional procedures. When compared to other procedures, one of the greatest benefits of IL is the availability of multiple repetition with minimal complication. Most of our patients preferred IL because of its minimal invasiveness and ease of procedure. Moreover, many reports showed comparable postoperative voice results of IL compared to medialization thyroplasty. Therefore, in these days, we rarely recommend medialization thyroplasty unless IL is not feasible for some technical reasons. Regarding to selecting repeated IL or arytenoid adduction as an additional procedure, we recommended arytenoid adduction if there are large posterior glottal gap or significant vertical height mismatch between the vocal folds. In addition, arytenoid adduction was recommended when patients demanded a relatively stronger and louder voice because of their occupation or noisy environment.

We used ArteSense for the purpose of vocal fold augmentation since the year 2005. It is classified as a long-lasting injection material for the soft tissue augmentation reportedly lasting up to 15 years. The collagen in ArteSense is readily absorbed within a month and it stimulates patients’ own neo-collagenesis. It allows slow tissue ingrowth over 3 months into the interstitial space around the PMMA microspheres, which results in long-lasting volume augmentation. Because of these characteristics of ArteSense, we have a principle that additional intervention should be at least 3 months apart from the initial IL. In most cases, we performed the additional injection 3–10 months after the initial IL. Average time interval between the injections was 8 month with the range of 1–52 months.

There are several limitations in this study. We used ArteSense for both the first and second IL regardless of the possibility of spontaneous recovery from vocal fold paralysis. Since we did not evaluate the effects of other injection materials, voice outcomes might be different if a temporary material was used for the first IL and a permanent material for the second IL, which is the common pattern of practice in treating the vocal fold paralysis of unknown possibility of recovery. Nevertheless, this study showed that a repeated IL with the same long-lasting material could provide further voice improvement especially in patients’ subjective perception without any significant side effects. Voice evaluations were routinely performed before and at 3–6 months after IL. If there is no need for the additional intervention, the patients were followed up at 1 year after IL with laryngoscopic evaluation only. Therefore, we could not provide the objective long-term data of additional IL even though we used a long-lasting material for the IL. Laryngeal stroboscopic findings were not statistically analyzed in this study even though stroboscopic findings (patterns of glottal closure, size of glottic gap, vertical level difference, vocal atrophy, and compensatory contraction of the supraglottic structures) were important references for the decision of next treatment including voice therapy, injection laryngoplasty, and/or laryngeal framework surgery. In addition, we did not use validated objective tools for evaluating the degree of aspiration or dysphagia. Therefore, we could not provide quantitative data on swallowing impairment in this study.

CONCLUSION

In selected patients, additional IL could provide further improvement of voice in those who had unsatisfactory voice results after initial IL. Among evaluated voice parameters, subjective perception (VHI-30) significantly improved by additional IL than by initial IL.
BIBLIOGRAPHY