

Office-Based Autologous Fat Injection Laryngoplasty for Glottic Insufficiency in Patients Under 50 Years Old

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Summary: Objective. We sought to determine the outcomes of office-based autologous fat injection laryngoplasty in the treatment of patients under 50 years old with glottic insufficiency but without neurological problems or acquired organic lesions in the vocal fold.

Methods. We conducted a retrospective chart review of consecutive patients under 50 years of age who underwent office-based autologous fat injection laryngoplasty for glottic insufficiency. None of the patients presented neurological problems or acquired organic lesions in the vocal fold. Videolaryngostroboscopic data, objective voice assessment, perceptual measurements of vocal quality, and subjective ratings of voice quality were evaluated before and after treatment.

Results. The 23 patients (7 men and 16 women) in this study presented significant improvements in phonatory function in terms of maximum phonation time, jitter, grade, asthenia, and Voice Handicap Index-10 (VHI-10) values at 3 months. Significant improvements in terms of jitter, noise-to-harmonic ratio, grade, roughness, breathiness, asthenia, and the VHI-10 values were also observed at 6 months.

Conclusions. Glottic insufficiency in younger patients without neurological problems or acquired organic lesions in the vocal fold can be treated effectively using office-based autologous fat injection laryngoplasty. Significant improvements in phonatory function were observed even 6 months after surgery.

Key Words: Glottic insufficiency—Injection laryngoplasty—Autologous fat—Office-based surgery—Younger patients.

INTRODUCTION

Glottic insufficiency, caused by unintentional air escape during normal phonation, can result in hoarseness, vocal fatigue, neck muscle tenderness, odynophagia, and susceptibility to choking.¹ Vocal fold paralysis, atrophy, and organic lesions could result in glottic insufficiency. However, at our voice clinic, a stroboscope has been used to help diagnose a number of relatively young patients presenting with glottic insufficiency but without neurological problems or acquired organic lesions in the vocal fold. The effects of dysphonia caused by glottic insufficiency tend to be more consequential in younger populations due to the fact that most of these individuals are still of working age.

Injection laryngoplasty is meant to restore glottal closure and is the most common intervention used in the treatment of glottic insufficiency.² A number of materials can be used for injection laryngoplasty; however, autologous fat is universally available and seldom induces rejection reactions. The feasibility of using autologous fat injection laryngoplasty in the treatment of glottic insufficiency has been reported in several articles.^{3–6} Nonetheless, the treatment outcomes of young patients undergoing office-based autologous fat injection laryngoplasty for glottic insufficiency have yet to be fully elucidated. In this study, we evaluated the treatment outcomes of office-based autologous fat injection laryngoplasty when administered to patients who were under the age of 50 and did not present neurological problems or acquired organic lesions in the vocal fold.

MATERIALS AND METHODS

In this study, we conducted a retrospective review of consecutive patients who (1) were under the age of 50; (2) suffered from glottic insufficiency without neurological problems or acquired organic lesions in the vocal fold; and (3) underwent office-based autologous fat injection laryngoplasty at the voice center of Cheng Hsin General Hospital with regular follow-ups between February 2015 and July 2016. This study was approved by The Institutional Ethics and Research Committee of the Cheng Hsin General Hospital.

A flexible laryngovideoscope indicated a diagnosis of glottic insufficiency in patients who reported subjective laryngological complaints such as hoarseness, vocal fatigue, neck muscle tenderness, odynophagia, and susceptibility to choking. The patients included in this study presented an elliptical closure gap, an anterior closure gap, or a glottic cycle wherein $\leq 40\%$ of all frames were in the closed phase (based on a frame-

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Study concept and design: Dr. Hu and Dr. Chang.

Acquisition, analysis, and interpretation of data: All authors.

Drafting of manuscript: All authors.

Critical revision of manuscript for important intellectual content: Dr. Chang.

Statistical analysis: Dr. Hu and Dr. Tung.

Administrative, technical, and material support: Ms. Hun and Ms. Lin.

Study supervision: Dr. Chang.

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FIGURE 1. Curved 18-gauge needle used to inject autologous fat.

by-frame analysis).¹ The patients did not present acquired organic lesions (eg, vocal fold polyps, vocal fold nodules, vocal fold cysts, vocal fold leukoplakia, polypoid vocal folds), neurological problems of the larynx (eg, vocal fold paralysis, spasmodic dysphonia, Parkinson's disease), or a history of malignant tumors in the larynx or pharynx. Patients who had previously undergone surgery or other procedures in treating the larynx were also excluded.

In our clinic,⁷ autologous fat injection laryngoplasty involves harvesting fat tissue from the low abdomen using a 3-mm liposuction cannula under local anesthesia. Following this, topical anesthesia (4% lidocaine hydrochloride solution) is administered to the nasal cavity, pharynx, and larynx, and fat is then injected into the bilateral vocalis muscle via the thyrohyoid membrane using a curved 18-gauge needle (Figure 1), with the injection process monitored by videolaryngoscopy. In this study, a total of 0.5 mL of fat was injected into three points of each vocal fold, and the entire procedure was completed within 30 minutes. Following surgery, all patients were instructed to rest their voices for 2 days. Voice therapy and antireflux medication were prescribed for 1 month following the injection. Conditions related to vocal fold vibrations were evaluated by videolaryngostroboscopy at 1, 3, and 6 months

following the procedure. In case of inadequate augmentation, a repeat injection would be performed no less than 3 months after the initial procedure, in accordance with clinical conditions following stroboscopic evaluation.

Acoustic recordings and phonatory function were evaluated by two speech pathologists before and after the procedure. A computerized speech laboratory (model 4500; KayPENTAX) was used to analyze 3-second samples of voice data, in which jitter, shimmer, and noise-to-harmonic ratio (NHR) values were tabulated. Maximum phonation time (MPT) was measured using a display that showed the waveforms of acoustic signals. Perceptual ratings of voice quality (based on grade, roughness, breathiness, asthenia, and strain,⁸ ie, GRBAS ratings) were independently evaluated by two speech pathologists in a blind procedure. The Voice Handicap Index-10 (VHI-10) questionnaire⁹ was used to collect subjective ratings from patients.

All statistical analyses were performed using SPSS version 18.0.0 (SPSS, Inc., Chicago, IL). Paired t-tests were used to analyze paired data. Continuous data are presented as mean \pm standard deviation. Statistical significance was set at a level of $P \leq 0.05$.

RESULTS

This study included 7 male and 16 female patients (mean age, 39.2 years; age range, 26–49 years). Four patients also presented with sulcus vocalis. Two of the patients underwent office-based autologous fat injection laryngoplasty a second time, after the first injection was shown not to provide adequate augmentation. All patients tolerated the procedures, and no complications were reported in this series.

Table 1 lists the results of voice laboratory measurements, perceptual measurements of vocal quality, and subjective evaluations by patients. Postoperative values obtained at 3 months revealed significant improvements in terms of MPT, jitter, grade, asthenia, and VHI-10 values compared with values obtained preoperatively. Postoperative values obtained at 6 months showed significant improvements in terms of jitter,

TABLE 1.
Results of Phonatory Function Evaluations

| | Mean \pm SD | | | P Value | | |
|-------------|-------------------|--------------------|--------------------|--------------------------|------------------|--------------------------|
| | Preoperative | Postoperative 3 Mo | Postoperative 6 Mo | Preoperative Versus 3 Mo | 3 Mo Versus 6 Mo | Preoperative Versus 6 Mo |
| MPT (s) | 11.67 \pm 6.95 | 13.40 \pm 7.20 | 13.08 \pm 7.20 | 0.032* | 0.678 | 0.181 |
| Jitter (%) | 1.85 \pm 1.85 | 0.75 \pm 0.57 | 0.76 \pm 0.53 | 0.012* | 0.961 | 0.007* |
| Shimmer (%) | 5.21 \pm 6.18 | 3.20 \pm 1.48 | 3.03 \pm 1.46 | 0.144 | 0.471 | 0.090 |
| NHR | 0.17 \pm 0.11 | 0.12 \pm 0.02 | 0.12 \pm 0.03 | 0.052 | 0.494 | 0.034* |
| Grade | 1.59 \pm 0.42 | 1.28 \pm 0.36 | 1.33 \pm 0.36 | 0.002* | 0.604 | 0.015* |
| Roughness | 1.48 \pm 0.35 | 1.30 \pm 0.33 | 1.20 \pm 0.29 | 0.103 | 0.233 | 0.004* |
| Breathiness | 1.26 \pm 0.45 | 1.04 \pm 0.45 | 0.91 \pm 0.51 | 0.096 | 0.342 | 0.015* |
| Asthenia | 1.43 \pm 0.46 | 1.07 \pm 0.27 | 1.07 \pm 0.23 | 0.004* | 1.000 | 0.001* |
| Strain | 1.28 \pm 0.70 | 1.17 \pm 0.63 | 1.04 \pm 0.42 | 0.565 | 0.418 | 0.178 |
| VHI-10 | 19.87 \pm 10.26 | 12.09 \pm 9.78 | 7.61 \pm 6.70 | <0.001* | 0.024* | <0.001* |

* A P value of ≤ 0.05 was considered statistically significant.
Abbreviation: SD, standard deviation.

NHR, grade, roughness, breathiness, asthenia, and VHI-10 values compared with values obtained prior to the procedure. Overall, voice laboratory measurements and perceptual measurements of vocal quality recorded at 6 months were comparable with those recorded at 3 months. However, subjective evaluations (obtained using the VHI-10 questionnaire) suggest that the improvements at 6 months were significantly more pronounced than those at 3 months.

DISCUSSION

Glottic insufficiency can be treated using voice therapy, injection laryngoplasty, and laryngeal framework surgery. Voice therapy has proven quite effective in addressing many of the conditions associated with glottic insufficiency.^{10–12} However, Gartner-Schmidt and Rosen reported that, in many cases, the voice may actually sound worse after secondary larynx hyperfunction is decreased via voice therapy.¹³ Furthermore, in one previous study, 94% of patients with glottic insufficiency related to vocal fold atrophy presented abnormal muscle tension patterns in the larynx.¹⁴ For these reasons, we generally prefer to augment voice therapy with injection laryngoplasty.

Injection laryngoplasty is the mainstay surgical treatment for glottic insufficiency.¹⁵ Numerous substances can be used for injection; however, autologous fat is nearly universal in availability as it can be harvested directly from the patient. Autologous materials greatly reduce the likelihood of inflammation and rejection reactions, and the relatively low viscosity of autologous fat is similar to that of vocal fold tissue, which could reduce the difficulties involved in phonation.¹⁶ Furthermore, adipose-derived stem cells (ASCs) can be found in grafted fat³ 3 months after transplantation.¹⁷ ASCs promote the survival of grafted adipose tissue and contribute to ongoing vocal fold remodeling through the release of proangiogenic paracrine growth factors, including vascular endothelial growth factor, basic fibroblast growth factor, hepatocyte growth factor, and insulin-like growth factor-1.¹⁸ Administering growth factor therapy to patients with vocal fold atrophy has resulted in the favorable recovery of vibratory characteristics as well as improved aerodynamic and acoustic functions.¹⁹ The response of vocal fold fibroblasts to stimulation from growth factors released by ASCs is also more pronounced in younger populations.²⁰ This is a clear indication that autologous fat is suitable for injection laryngoplasty in younger patients.

Nonetheless, there is always the risk of autologous fat being reabsorbed after injection. The degree of volume loss following this type of lipotransfer ranges from 20% to 90%,²¹ and most reabsorption occurs in the first 2 months after surgery.²² The complete remodeling of grafted fat requires approximately 3 months.^{17,23} Grafted fat that survives this initial period can last for up to 3 years²³ and may therefore be considered a permanent filler.²³ Injections may be repeated (if needed) but not until at least 3 months have elapsed after the initial procedure. Further studies will be required to develop methods that can enhance the survival of grafted fat.

Office-based laryngeal surgeries lack the precision of procedures that involve general anesthesia; however, they have been

proven worthwhile alternatives in recent years.^{7,24,25} Indeed, office-based injection laryngoplasty has been shown to be safe and relatively inexpensive.^{26,27} Unfortunately, the relatively large needle required for fat injection (18-gauge in our series) may induce considerable discomfort during the procedure, especially when compared with the smaller needles used to inject other substances. The success of office-based autologous fat injection laryngoplasty depends on the tolerance of the patient to the procedure. Prior to administering the injection, surgeons should explain the procedure in detail and prepare the patient for the discomfort they are likely to endure.²⁶ In addition, the procedure should be performed by experienced surgeons due to the fact that the stability of patients gradually decreases during prolonged procedures under topical anesthesia.²⁴ The fact that all of the patients in our series readily tolerated office-based autologous fat injection laryngoplasty may be regarded as an indication of the feasibility and safety of this procedure. Furthermore, we found that office-based procedures that employ topical anesthesia are preferred for patients who require repeat procedures due to inadequate vocal fold augmentation. Finally, patients who undergo less complex treatments (compared with surgeries under general anesthesia) tend to have more realistic expectations of treatment outcomes.

The treatment of glottic insufficiency without neurological problems or acquired organic lesions in the vocal fold poses a number of daunting challenges. For example, the symptoms associated with this condition are subtle at presentation, and the overall changes that occur after intervention tend to be indistinct. Discrepancies in the outcomes among various series (both conservative methods and surgical treatments) have caused some controversy.^{10,13,28} Unsatisfactory improvements are particularly evident in cases where patients undergo surgical intervention under the false expectation that surgery offers an ultimate fix.¹³ In our experience, we observed an overall improvement in voice quality in our series of office-based autologous fat injection laryngoplasty administered in conjunction with voice therapy. Indeed, significant improvements in phonatory function could still be noted at 6 months after the intervention. We posit that the different outcomes reported by various series can be attributed to the fact that the patients investigated in these series were not of the same age with glottic insufficiency. To the best of our knowledge, this current study is the largest reported case series on office-based autologous fat injection laryngoplasty for the treatment of glottic insufficiency in younger patients.

Interestingly, in our series, we observed no significant changes in laboratory voice measurements or in perceptual measurements of vocal quality between 3 and 6 months; however, our VHI-10 values were better at 6 months than at 3 months. We speculate that these improvements in subjective VHI-10 values may be related to a number of factors. First, the patient may present with an unstable voice until fat remodeling is completed after 3 months due to ongoing, dynamic changes in adipose tissue.¹⁷ Thus, the results of objective voice examinations (performed by a speech pathologist) were similar at 3 and 6 months. In contrast, the subjective questionnaire from which VHI-10 values are determined is based on patients' evaluation

of their own voice function according to “recent” experience. It is therefore reasonable to expect patients to consider the unstable voice condition that characterizes the initial period after surgery in their subjective evaluation at 3 months. In contrast, the subjective evaluation at 6 months would likely be based on the relatively stable voice condition typical of patients 3–6 months after surgery. Second, many patients no doubt require at least 6 months to become familiar with the augmented vocal folds and decreased larynx hyperfunction that occur following voice therapy. Third, growth factors released by ASCs may contribute to ongoing vocal fold remodeling. Even when growth factors do not result in obvious changes in voice measurements over the short term, patients may still experience subtle but gradual improvements.

This study was limited by the small number of patients in the cohort and the lack of control groups. Additional studies will be required to further validate our approach as well as the procedural details of injection as a therapeutic strategy. Furthermore, we cannot rule out the possibility that the voice therapy undertaken by the patients in this study influenced our results. Additional research will be required to clarify this potential bias. Finally, we included only younger patients with glottic insufficiency in this series. Further studies will be needed to investigate treatment outcomes in different age groups.

CONCLUSIONS

Office-based autologous fat injection laryngoplasty is a reasonable strategy for the treatment of glottic insufficiency among patients under 50 years of age who do not present neurological problems or acquired organic lesions in the vocal fold. The patients in this study presented improvements in voice laboratory measurements, perceptual measurements of vocal quality, and subjective evaluations of voice quality. Significant improvements in phonatory function were still noted at 6 months after surgery.

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