

Phonosurgical Injection Approaches for Voice Restoration After Open Partial Horizontal Laryngectomies: A Pilot Study

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Summary: Objective. The aim of the present study is to evaluate the efficacy of phonosurgical corrective approaches based on injection laryngoplasties and pharyngoplasties followed by speech therapy for voice restoration after unsatisfactory phonatory results of open partial horizontal laryngectomies.

Methods. Ten patients with not satisfying phonatory results despite speech therapy after type II or type III open partial horizontal laryngectomies (OPHLs) were included. Each patient underwent a voice restoration program based on phonosurgery (injection laryngoplasty and/or injection pharyngoplasty) with hyaluronic acid and/or calcium hydroxyapatite, followed by post-surgical voice rehabilitation. Voices were recorded and analysed through spectrographic, aerodynamic, perceptual, laryngoscopic and self-assessment evaluations before the treatment (T0), after 1 month (T1) and after three months (T2).

Results. Significant improvements in the patients voices were found between T0, T1 and T2 concerning acoustic, perceptual, aerodynamic, laryngoscopic and self assessment evaluations.

Conclusions. The results of the present study support phonosurgical injection procedures followed by speech therapy as an effective strategy for voice restoration after type II or type III OPHLs in selected patients.

Key Words: Phonosurgery—Voice—Laryngectomy—Laryngeal cancer—Rehabilitation.

INTRODUCTION

Voice can be severely affected after surgical and non-surgical treatments for laryngeal cancer, with a negative impact on voice and communication-related quality of life. Several options are available today for the treatment of laryngeal cancer, including surgical and nonsurgical approaches. Among these, open partial horizontal laryngectomies (OPHLs) represent a system of modular function sparing surgical approaches for the treatment of early-intermediate and selected advanced laryngeal carcinomas, allowing the preservation of the main laryngeal functions and avoiding a permanent tracheostoma.^{1,2}

According to the OPHL classification system proposed by Succo et al,³ three types of open partial horizontal laryngectomies can be described: type I (supraglottic laryngectomy); type II (supracricoid laryngectomy) and type III (supratracheal laryngectomy). Type I OPHLs spare the glottic plane and usually have good phonatory outcomes, with satisfactory voice quality.^{4,5} Besides, type II and type III OPHLs, entailing respectively supracricoid and supratracheal resections, sacrifice both vocal folds and require the creation of a neoglottis, with a deep impact on voice. After type II and

type III OPHLs voice is usually similarly affected, with a hoarse, breathy and rough quality.⁶ Type II OPHLs spare at least one arytenoid (ARY); while type III OPHLs entail the resection of the cricoid ring, preserving at least one crico-arytenoid unit (CAU). When one arytenoid is resected in type II OPHLs, “+ ARY” is indicated; when one crico-arytenoid unit is resected in type III OPHL, “+ CAU” is indicated. Part of the epiglottis is preserved in type II/IIIa OPHLs while is completely resected in type II/IIIb OPHLs. Reconstruction of the airway is obtained through a crico-hyoido-epiglottopexy in type IIa OPHLs, with a crico-hyoidopexy in type IIb OPHLs, with a tracheo-hyoido-epiglottopexy in type IIIa OPHLs and with a tracheo-hyoidopexy in type IIIb OPHLs.

As previously described by some authors, phonosurgical approaches based on injection laryngoplasties (ILs) and injection pharyngoplasties (IPs) can be very useful for the correction of functional insufficiency of the neoglottis.⁷ ILs are performed through injections in the residual laryngeal structures, mainly represented by arytenoids or crico-arytenoid units; IPs usually consist of injections in the base of tongue or in the residual hypopharyngeal mucosa. Ricci Maccarini et al. firstly described the possibility of a surgical rehabilitation of dysphagia after partial laryngectomy by means of injection laryngoplasties and pharyngoplasties, that can be performed booth by direct microlaryngoscopy (DML) under general anesthesia and by trans-nasal fiber endoscopic phonosurgery (FEPS) under local anesthesia. The authors suggest that ILs and IPs might represent a good solution for treating dysphagia after open partial horizontal laryngectomies.⁸ To date, no systematic data exist in literature about the results of such technique on voice quality improvement after OPHLs.

The aim of the present study is to evaluate the efficacy of phonosurgical corrective approaches based on injection

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laryngoplasties and/or pharyngoplasties followed by speech therapy for voice restoration after unsatisfactory phonatory results of type II and type III OPHLs.

MATERIALS AND METHODS

The present study was carried out according to the Declaration of Helsinki and it was previously approved by the Institutional Review Board. All data were collected retrospectively.

Patients and procedures

Ten patients (5 males and 5 females) who underwent type II or type III OPHL were phonosurgically treated with injection procedures between 2018 and 2020 at the Head and Neck Department of FPO-IRCCs Candiolo Cancer Center and were identified in a database of more than 1000 patients who underwent OPHL between 2004 and 2018. Sociodemographic and clinical features of the sample are shown in [Table 1](#). Mean age was 69 ± 2 years and mean time after surgery at the last functional assessment was 43 ± 29 months.

Selection criteria for phonosurgery were: previous OPHL, no evidence of disease (NED) and laryngeal function preservation (LFP) at the last follow-up (preservation of respiration, speech and oral feeding without percutaneous endoscopic gastrostomy or naso-gastric tube, absence of tracheostoma, no salvage total laryngectomy performed), > 6 months after surgery, not satisfactory voice outcome - despite a regular postoperative speech therapy rehabilitation - according to a multidimensional analysis based on aerodynamic, electroacoustic, perceptual, self assessment and endoscopic evaluations. All patients underwent the same preoperative and post-operative course as described by Rizzotto et al.⁹

The patients included in the present study underwent injection laryngoplasty and/or pharyngoplasty procedures with cross-linked hyaluronic acid (HA) (Restylane,

Galderma SA, Zug, Switzerland) through fiber endoscopic phono-surgery (FEPS) under local anesthesia using a Karl STORZ flexible operative rhinolaryngoscope (KARL STORZ SE & Co. KG, Tuttlingen, Germany) and 19 gauge 80 cm long flexible endoscopic needles (BTC Medical Europe, Valeggio sul Mincio, Verona, Italy) or with calcium hydroxyapatite (CaHA) (Rénu Voice, Soluvos Medical Ltd, London, UK) and HA through direct micro-laryngoscopy (DML) procedures under general anesthesia using a Karl STORZ Lindholm laryngoscope and rigid endoscopic injection needles (KARL STORZ SE & Co. KG, Tuttlingen, Germany). The amount of the injected materials was 2 ml for HA and 1.5 ml for CaHA.

The choice of the surgical approach was defined during the preoperative evaluations and was made according to the selected site of injection and type of OPHL. In particular, eight patients underwent FEPS procedures under local anesthesia. In these cases, HA was injected in the mucosa of the residual ARYs/CAUs. Two patients who previously underwent a type IIb OPHL and needed a corrective injection in the base of tongue, underwent DML procedures with both injection laryngoplasty with HA in the residual ARYs and injection pharyngoplasty with HA and CaHA in the base of tongue. Such site of injection, because of the fibrous scarring processes occurring after the crico and/or tracheo-hyoidopexy, cannot be easily reached and injected through a flexible trans-nasal fiber endoscopic approach. Moreover, cross linked HA alone might not provide a satisfactory and long lasting filling effect at this particular site. For this reason, a DML under general anesthesia using both cross linked HA and CaHA was preferred. Examples of ILs and IPs performed by DML and FEPS are shown in [Figure 1](#). No postoperative complications were registered.

Each patient underwent a transnasal fiber endoscopic evaluation at 7 days after surgery in order to check the immediate postoperative course and exclude post-surgical complications. Then, each patient underwent a voice rehabilitation protocol of 2 months based on the Proprioceptive Elastic (PROEL) method, as described in a previous study.¹⁰ Checkpoints for voice outcomes evaluation were at 1 month and at 3 months after surgery.

All the following assessments were carried out before phonosurgery (T0), 1 month after surgery (T1) and 3 months after surgery (T2). The only exception was represented by the self-assessment questionnaire, which was administered at T0 and T2.

Voice analysis

Voice signals were recorded respecting standard conditions, with a Samson Meteor Mic (Samson Technologies, Hauppauge, NY) placed at a distance of 30 cm from the mouth of the Patient in a quiet environment (<40dB), connected via USB to a MacBook Pro computer (Apple, Cupertino, CA) running PRAAT software (Version 5.3.57 for Mac, Boersma & Weenick, University of Amsterdam,

TABLE 1.
Sociodemographic and Clinical Features of the Sample

N. patients	10
Age (years)	69 ± 2
Sex (n. and %)	
Male	5 (50%)
Female	5 (50%)
Distance from surgery (months)	43 ± 29
Type of surgery	
OPHL IIa	1 (10%)
OPHL IIa + ARY	4 (40%)
OPHL IIb	1 (10%)
OPHL IIb + ARY	1 (10%)
OPHL IIIa	2 (20%)
OPHL IIIa + CAU	1 (10%)

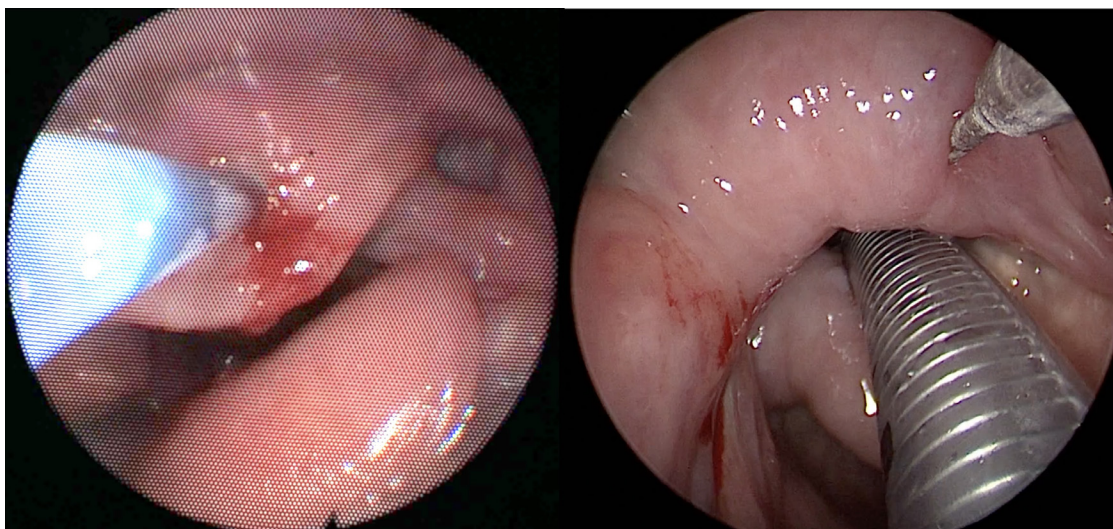


FIGURE 1. Examples of an injection laryngoplasty procedure conducted under local anesthesia by FEPS (left) and an injection pharyngoplasty procedure conducted under general anesthesia by DML (right). On the left, injection is being performed in the mucosa of a residual ARY after a type IIa OPHL + ARY. On the right, injection is being performed in the base of tongue after a type IIb OPHL.

Amsterdam, the Netherlands). Audio files were digitized on 16 bit at sampling frequency of 48 kHz.

Maximum phonation time (MPT) was measured through the window selection of the longest of three sustained /a/. Spectrograms of the sustained vowel /a/ were obtained with a frequency range of 0-5000Hz and calculated with a 0.05 seconds window length and a 45 dB dynamic range.

Patients' voices were classified into four categories on the basis of the spectrogram analysis, according to the proposed modified Titze's classification.¹¹ The following categories were used:¹ type I voices, periodic without strong modulations or subharmonics;² type II voices, with strong modulations, bifurcations, or subharmonics;³ type III voices, smearing of energy across harmonics with visible fundamental frequency and 1 or 2 harmonics;⁴ type IV voices, aperiodic.

Perceptual assessments were carried out with the INFVo rating scale, a perceptual scale specifically developed for substitution voice, assessing overall quality impression and intelligibility (I), additive and unnecessary noise (N), speech fluency (F), and presence of voiced segments (Vo).¹² Each parameter is scored on a visual analog scale from 0 (minimally deviant) to 10 (maximally deviant substitution voicing). The perceptual evaluation was performed by listening to a recorded 56-word and 99-syllable passage. All voice recordings were blindly assessed and rated by two experienced and trained speech and language pathologists.

Videolaryngoscopies

Endoscopies were conducted with an Olympus Evis Exera II 18 endoscopy system and an Olympus ENF VQ trans-nasal flexible endoscope (Olympus Corporation, Tokyo, Japan).

The patients were asked to produce the following phonatory tasks: a sustained /i/, a low-pitched /i/, a high-pitched /i/, a low-intensity /i/, and a high-intensity /i/. The following variables were assessed:¹ vibratory characteristics of the neoglottis (A);² degree of arytenoids motion (B); and³ sphincteric closure of the larynx (C). Each variable was scored on a 5 point rating scale from 1 (poor performance) to 5 (excellent ability), as suggested by Zacharek et al.¹³

Voice and communication-related quality of life assessment

Each patient completed the Italian version of the Self-Evaluation of Communication Experiences after Laryngeal Cancer (I-SECEL).^{14,15} The I-SECEL questionnaire specifically assesses the impact of communication dysfunction on daily activities in patients who underwent laryngectomy. The questionnaire is made up of 34 items divided into 3 subscales: General (5 items), Environmental (14 items), and Attitudinal (15 items). Scores range from 0 to 102 for the total score, from 0 to 15 for the general subscale, from 0 to 42 for the environmental subscale, and from 0 to 45 for the attitudinal subscale. The higher the score, the greater the perception of communication dysfunction.

Statistical analysis

Statistical analysis was carried out with GraphPad Prism software (Version 7.0, Apple, Cupertino, CA). Means and standard deviations (SDs) for continuous variables were calculated. The normality of the distributions was assessed with the D'agostino Pearson Test.

Voice variables before and after phonosurgical approaches and voice therapy were calculated and compared. Friedman tests with Dunn's post hoc corrections for

multiple comparisons and ANOVA tests with Tukey's post hoc corrections for multiple comparisons were used to detect statistical differences between more than two groups, as appropriate. Paired *t* tests and Wilcoxon tests were used to compare outcomes between two groups, as appropriate. An alpha of 0.05 was considered for the statistical procedures.

RESULTS

Acoustic-aerodynamic analysis

Means and SD for MPT were 5.6 ± 3.1 seconds at T0; 6.4 ± 3.2 seconds at T1; 7.9 ± 3.7 seconds at T2, as shown in Figure 2. Significant differences were found between T0 - T1 ($P = 0.02$), T1 - T2 ($P = 0.03$) and T0 - T2 ($P = 0.01$). Means and SD for Titze's modified Spectrographic class were 3.6 ± 0.5 at T0; 3.2 ± 0.6 at T1; 2.7 ± 0.5 at T2, as shown in Figure 3. Significant differences were found between T0 and T2 ($P = 0.007$).

Perceptual analysis

Means and SD for the INFVo rating scale are shown in Table 2. All the subscales showed significant differences. In particular, post hoc tests showed significant differences between T0 and T1 for the subscales I ($P = 0.001$), N ($P = 0.02$), Vo ($P = 0.04$); between T1 and T2 for the subscales I ($P = 0.001$), N ($P = 0.04$), Vo ($P = 0.04$); between T0 and T2 for the subscales I ($P < 0.001$), N ($P = 0.002$), Vo ($P = 0.01$). No significant difference was found for the subscale F at any checkpoint.

Videolaryngoscopies

Means and SD for the videolaryngoscopic variables are shown in Table 3. Significant differences were found for the vibratory characteristics of the neoglottis (A) between T0-T2 ($P < 0.001$); for the degree of arytenoids motion (B) between T0-T2 ($P = 0.009$) and T1-T2 ($P = 0.01$); for the sphincteric closure of the larynx (C) between T0-T1 ($P = 0.03$) and T0-T2 ($P = 0.02$). Two examples of improved neoglottic closure during phonation after phonosurgery are shown in Figure 4.

Self assessments

Means and SD for the SECEL questionnaire at T0 were: T = 40 ± 10.9 ; G = 9.2 ± 2.1 ; E = 15.6 ± 5.3 ; A = 9.2 ± 4.8 . Means and SD at T2 were: T = 33.1 ± 10.2 ; G = 10 ± 1.9 ; E = 20.8 ± 7.8 ; A = 7.5 ± 4.8 . Significant differences were found between T0 and T2 for the subscales: Total score ($P = 0.02$) and Environmental ($P = 0.01$).

DISCUSSION

The present study shows a case series of ten patients with unsatisfactory voice results after type II and type III OPHL, who underwent phonosurgery (injection laryngoplasties and/or pharyngoplasties) followed by speech therapy. Multidimensional voice assessments showed significant improvements regarding acoustic-aerodynamic analysis, perceptual evaluations, laryngoscopic findings and self assessments. MTP significantly improved at T1 and at T2 suggesting better neoglottic competence during phonation. At the same time, a significant improvement in the

Maximum Phonation Time (MPT)

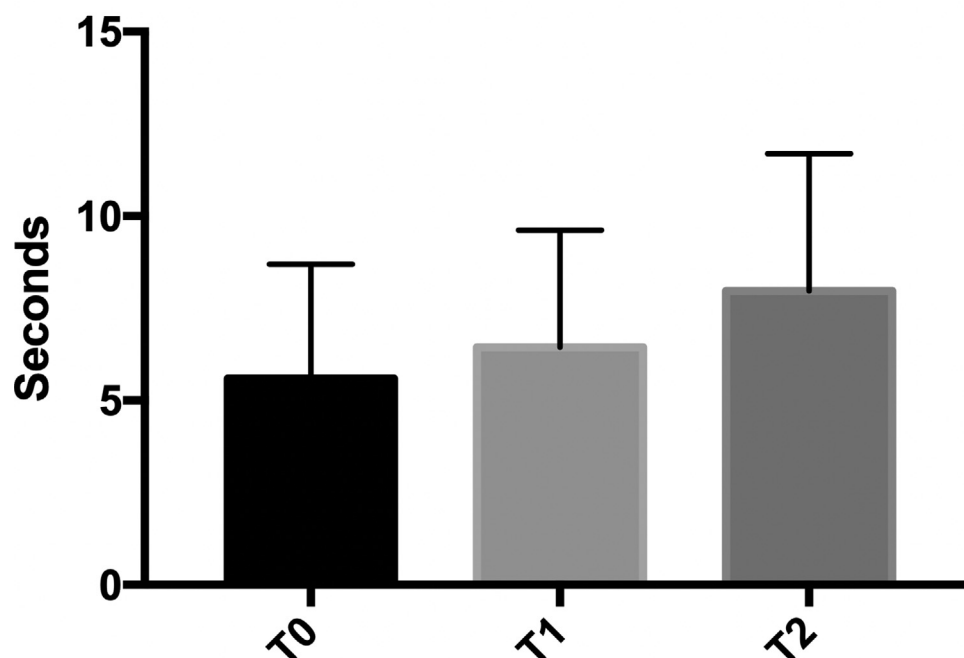


FIGURE 2. Mean values of Maximum Phonation Time at T0, T1 and T2.

Spectrogram

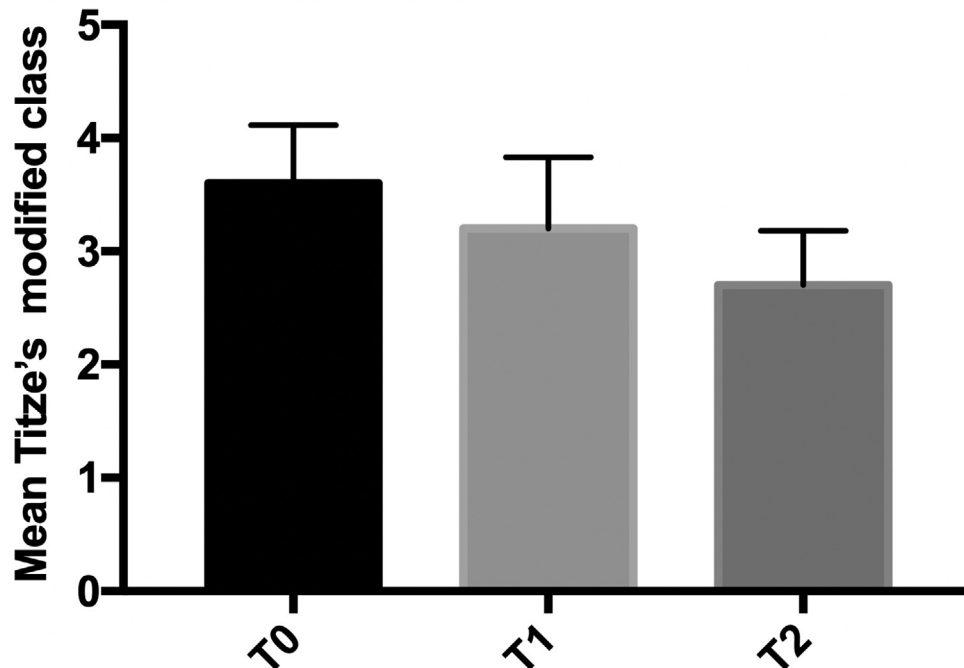


FIGURE 3. Mean values of Titze's modified spectrographic classification at T0, T1 and T2.

spectrographic features was found between T0 and T2, reflecting a finer vibration of the neoglottis. Such results are strengthened by the laryngoscopic findings, confirming better closure, motion and vibration of the neoglottis after the treatment. Concerning perceptual evaluations, the patients' voices showed significant improvements for the following INFVo subscales: overall quality impression and intelligibility (I), additive and unnecessary noise (N) and presence of voiced segments (Vo). A significant reduction of the total score (T) and environmental subscale (E) of the self

assessment questionnaire SECEL were found too, suggesting a mean better communication-related quality of life.

The results of the present study suggest that a combined approach based on injection phonosurgical procedures and speech therapy might represent a valid strategy for voice restoration in patients with unsatisfactory voice results after type II/type III OPHL despite speech therapy alone. To the best of our knowledge, this represents the first study to investigate systematically and multidimensionally the results of such treatments on voice after OPHLs. Some other

TABLE 2.
Mean Values, Standard Deviations, Test and p-value of INFVo Subscales at T0, T1 and T2

Subscale	T0 (Mean and SD)	T1 (Mean and SD)	T2 (Mean and SD)	Test	P value
I	5.55 ± 2.55	4.50 ± 2.32	3.20 ± 1.75	RM One Way ANOVA	<0.001
N	5.00 ± 3.24	3.90 ± 2.47	2.80 ± 2.8		<0.001
F	4.00 ± 2.12	4.20 ± 2.53	3.90 ± 3.9		0.77
Vo	4.20 ± 4.08	3.20 ± 3.08	1.40 ± 1.4		0.004

TABLE 3.
Mean Values, Standard Deviations, Test and p-value of Videolaryngoscopic Variables at T0, T1 and T2

Subscale	T0 (Mean and SD)	T1 (Mean and SD)	T2 (Mean and SD)	Test	P value
A	1.4 ± 0.8	3.3 ± 1.1	2.8 ± 1.7	Friedman Test + Dunn's multiple comparisons test	<0.001
B	2.8 ± 0.4	3.5 ± 0.7	4.1 ± 0.6		0.002
C	3.7 ± 0.5	4.1 ± 0.6	4.3 ± 0.7		0.007

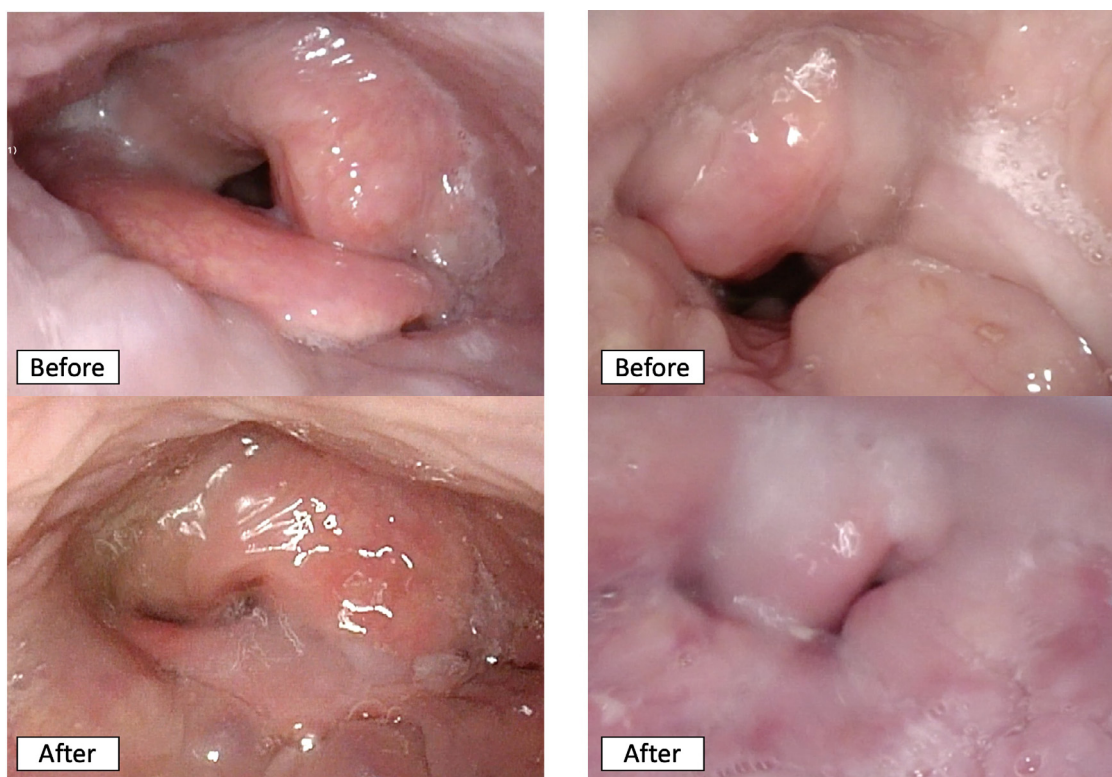


FIGURE 4. Examples of neoglottic phonatory competence improvement after phonosurgery. Left: type IIa + ARY OPHL; right: type IIb OPHL.

authors investigated surgical voice restoration strategies after conservative laryngeal surgery for laryngeal cancer. For example, Chirilă and colleagues proposed the use of tragal cartilage and perichondrium for voice rehabilitation after open partial vertical laryngectomies, placing a cartilage graft in a pocket of the neocord in order to obtain medialization and better glottic closure. The authors investigated phonatory outcomes in sixteen patients after 14 days, 60 days and 6 months, obtaining significant improvements concerning both voice quality and breathiness.¹⁶ Similarly, other authors investigated the effects of medialization laryngoplasty with Montgomery or Gore-Tex implants after type IV and V endoscopic CO₂ laser cordectomies, obtaining significant acoustic, aerodynamic, perceptual and self-assessment improvements of voice.^{17,18} Considering phonosurgical injection corrections of the neoglottis after open partial horizontal laryngectomies, previous studies mainly focused on the restoration of swallowing function. For example, Ricci Maccarini et al. investigated the effects of injection laryngoplasties with autologous fat, collagen or polydimethylsiloxane (PDMS) performed by DML or FEPS in 7 patients with persisting severe dysphagia after OPHLs, obtaining a complete recovery in 4 patients, who also experienced a phonatory improvement. Two patients experienced a partial recovery and only one patient did not benefit from the surgical treatment.⁸ As suggested by the authors, particular attention should be paid to the pexy status. In some cases of unsatisfactory functional results despite phonosurgery, open surgical corrective approaches should be taken into account. In particular, open surgical revisions of crico-hyoido-

or tracheo-hyoidopexy can be performed in order to obtain a more posterior positioning of the base of tongue and a better airway protection. Encouraging results regarding surgical rehabilitation of swallowing after OPHLs were confirmed by later studies by Bergamini et al.^{19,20} In particular, in a recent study the authors investigated long term results after surgical rehabilitation of swallowing with PDMS in 28 patients who underwent OPHLs. Both self assessments and fiberoptic endoscopic evaluation of swallowing (FEES) showed significant long term improvements, suggesting injection laryngoplasty as a good option for surgical rehabilitation of swallowing after OPHL.²⁰ A recent study by Alaskorov et al. investigated functional outcomes after HA injections by DML in patient with persisting dysphagia and dysphonia after partial laryngectomy procedures. Several types of partial laryngectomy were included in the study (open cordectomies, fronto-lateral vertical partial laryngectomies, extended supraglottic partial laryngectomies and supracricoid partial laryngectomies). The authors found both voice and swallowing improvements up to 24 months after surgery, suggesting HA as a good injection material after open partial laryngeal surgery. Concerning voice, the authors performed aerodynamic and acoustic analysis (using MPT and microperturbation parameters such as Jitt% Shimm% and NHR, respectively) as well as self assessments using the Voice Handicap Index (VHI) questionnaire.²¹

When considering patients who had vocal folds completely resected (as it is in the case of supracricoid and supratracheal partial laryngectomies) it is preferable not to use some of the standard tools for voice analysis. Classical

perturbation parameters such as Jitt% and Shimm% might not be appropriate for the detection of acoustic changes in the neo-voice signals. Similarly, the VHI questionnaire was developed and validated on patients with vocal folds pathologies, and should not be administered to patients with a neo-glottis. This is the reason why in the present study specific tools such as the SECEL questionnaire and the INFVo rating scale were selected.^{12,14}

CaHA and cross linked HA were the materials used for injection laryngoplasties and pharyngoplasties. When a long lasting filling effect was required (eg, in the base of tongue) CaHA was preferred for IPs; on the contrary, to obtain more mucosal debridement and pliability (eg, on the arytenoids), cross-linked HA was chosen for ILs. It must be considered that cross-linked HA is a completely reabsorbable material, while CaHA is a partially reabsorbable one. While in dysphagic patients the priority is to obtain a long lasting filling effect, in dysphonic patients both neoglottic closure and mucosal vibration dynamics have to be taken into account in order reach better voice outcomes. According to our short and medium-term results, voice improvements after injection procedures might be obtained thanks to three main effects: 1) Volumizing effect: the mucosal filling gives the patient an immediate result, since an easier neoglottic competence is achieved. This hypothesis is supported by better aerodynamic results (longer MPT) and by the improvement of the laryngoscopic parameter C (sphincteric closure of the larynx); 2) Debriding and trophic effect: the submucosal injection of HA makes the neoglottic mucosa more pliable and elastic, resulting in better vibratory dynamics. Such effect is supported by the improvement of the spectrographic features, the perceptual assessments through the INFVo scale and the laryngoscopic parameter A (vibratory characteristics of the neoglottis); 3) Proprioceptive stimulus: an easier neoglottic closure and better vibration give the patients a strong sensory-motor feedback. Such condition might presumably lead the patients to automatically look for an optimal neoglottic closure and vibration even when the gradual reabsorption of the injected material takes place. Better experiences regarding phonation and communication in everyday life are supported by the significant improvement of the SECEL questionnaire scores at T2.

It must be pointed out that the postsurgical rehabilitation process is crucial for the maintenance of the phonatory outcomes. As demonstrated in a previous study, proprioception and elasticity-based approaches (as in the PROEL method) represent optimal solutions for neo-voice rehabilitation after OPHLs.¹⁰

Looking case by case at the results, the overall impression of the authors is that patients who underwent type II/IIIb OPHLs (where epiglottis is completely resected) are more difficult to treat with success. In these cases, the base of tongue has to be injected, but a satisfying neoglottic competence is sometimes hardly obtained. Nonetheless, the small sample size and the lack of a multivariate analysis does not allow to generalize such statements at the moment.

The main limitations of the present study are represented by the small and heterogeneous sample, the lack of a randomized trial study design and the lack of a long-term follow-up. Future research should include more patients and should be conducted prospectively with randomized trial designs, in order to analyze and identify factors associated with a better voice outcome after treatment (eg, considering type of phonosurgical technique, type of injected material, type of OPHL resection etc). Furthermore, long term results should be investigated, in order to quantify the effect of the proposed treatments over a long period of time.

CONCLUSIONS

Voice quality represents one of the major issues after open partial laryngeal surgery. In a minority of cases, phonatory outcomes after type II and type III OPHLs might be not satisfactory despite speech therapy. The results of the present study are promising and suggest that corrective approaches based on injection laryngoplasties and/or pharyngoplasties followed by voice rehabilitation might represent effective strategies for voice restoration after OPHL in selected patients.

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