Original Article

Clinical and functional characteristics of lung surgery-related vocal fold palsy

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ABSTRACT

Background: Unilateral vocal fold paralysis (UVFP) caused by lung surgery is associated with prolonged hospital stay and increased postoperative comorbidities. We evaluated lung surgery-related UVFP and compared its characteristics with UVFP caused by esophageal and thyroid surgeries, as the most common surgical causes of UVFP. We also evaluated the outcomes of intracordal hyaluronate injection laryngoplasty in these patients.

Methods: Patients with surgery-related UVFP were evaluated by quantitative laryngeal electromyography, videolaryngostroboscopy, voice acoustic analysis, Voice Outcome Survey (VOS) questionnaire, and Short Form-36 Health Survey (SF-36) quality-of-life questionnaire. Data for the lung, esophageal, and thyroid surgery groups were compared and changes in outcome measurements induced by hyaluronate injection were compared among the three groups.

Results: A total of 141 patients were recruited, including 21, 46, and 74 in the lung, esophageal, and thyroid surgery groups, respectively. Compared with the other two groups, lung surgery patients had predominantly left-sided UVFP, less involvement of the external branch of the superior laryngeal nerve, and higher jitter. Most outcome measurements improved in all three groups after office-based hyaluronate injection, with the greatest improvement in jitter in the lung surgery group.

Conclusions: Lung surgery-related UVFP showed a distinct disease presentation, and patients' voice parameters and quality of life recovered dramatically after office-based

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hyaluronate injection. We recommend evaluation of lung surgery-related UVFP and early intervention, such as office-based hyaluronate injection, to improve patients' voice function and quality of life.

At a glance of commentary

Scientific background on the subject

Unilateral vocal fold paralysis (UVFP) is a relatively common comorbidity of lung surgery and associated with longer hospital stay and higher rate of post-operative complications. Lung surgery-related UVFP is seldom discussed and the benefits of early intervention for this comorbidity remain unclear.

What this study adds to the field

Lung surgery-related unilateral vocal fold paralysis (UVFP) has a distinct disease presentation as compared with other surgery-related UVFP. As compared with other UVFP, patients with lung surgery-related UVFP have greater improvements in voice and quality of life after office-based intracordal hyaluronate injection.

Among patients receiving lung surgery, 59% underwent surgery for lung cancer (49% for primary and 10% for metastatic lung tumor) and the remainder for non-tumor etiologies, such as inflammatory pulmonary disease, pneumothorax, and mediastinal tumors [1]. Recent use of low-dose chest computed tomography scans have enabled the detection of early-stage lung cancer, thus increasing the number of patients suitable for minimally invasive resection procedures [2]. Unilateral vocal fold paralysis (UVFP) is a relatively common comorbidity of lung surgery, with 1.2% of 2136 patients who underwent surgery for lung cancer reportedly developing UVFP [3]. Surgery-related UVFP was also associated with a high rate of aspiration pneumonia and a longer hospital stay [4]. However, although UVFP is an important issue for lung surgery, its disease characteristics and clinical presentation remain largely unaddressed. Furthermore, the potential benefits of early intervention, such as intracordal hyaluronate (HA) injection laryngoplasty, are unclear.

Iatrogenic UVFP is comprising of two types of nerve injuries. Sole injury of the recurrent laryngeal nerve (RLN) results in paralysis of the thyroarytenoid–lateral cricoarytenoid (TA–LCA) muscle complex, the primary vocal fold adductor, causing glottic insufficiency [5], while combining injury of the external division of the superior laryngeal nerve (eSLN) causes paralysis of the cricothyroid (CT) muscle, impairing vocal fold tension and leading to lowered pitch, monotone voice, voice fatigue, or hoarseness [6]. Lung surgery approaches within the thoracic cage could injure the RLN but spare the eSLN, while lung surgeries involving the apical area and lymph node dissection in the mediastinum [7] may be more likely to induce UVFP because of the proximity of the surgical margin to the RLN.

Laryngeal electromyography (LEMG) is the golden standard for diagnosing UVFP and predicting its prognosis [8], and quantitative LEMG was recently developed to allow the objective quantification of the remaining neuromuscular recruitment [9]. Quantitative LEMG has high diagnostic, functional, and prognostic values for UVFP, and can be used to evaluate the severity of neuromuscular impairment in the TA–LCA muscle complex [9,10]. Improved understanding of the incidence and characteristics of surgery-related vocal fold paralysis will help to assess the need for intraoperative monitoring and selection of the optimal therapeutic strategy [11].

Thyroid, esophageal, and lung surgeries are the main surgical causes of UVFP, accounting for 84% of surgery-related UVFP [12]. Although abundant data have been collected for other surgery types [12,13], lung surgery-related UVFP is seldom discussed. Lung surgery commonly causes pain in the thoracic cage and decreases the tidal volume, thus limiting the patient's cough function and general vitality [14]. In addition, a decrease in the respiratory force required for voice production caused by lung surgery might further impair the patient's voice function and associated activities of daily living. Given the importance of the disease characteristics in patients with lung surgery-related UVFP, we comprehensively analyzed the quantitative LEMG, glottal gap, acoustic voice analysis, voice-related quality of life, and health-related quality of life in these patients. We also compared the data for UVFP following lung, thyroid, and esophageal surgeries to define the unique properties of lung surgery-related UVFP. Finally, the outcomes following HA injection for UVFP were compared among surgery types.

Material and methods

Human subjects

Participants were enrolled from the otolaryngology outpatient clinics at the Chang Gung Memorial Hospital Medical Center, Linkou, from September 2011 to April 2017. Inclusion criteria were adults (>20 years old) diagnosed with UVFP that occurred after surgery, confirmed by laryngoscopy and needle LEMG. Exclusion criteria were membranous lesions of vocal fold, UVFP before surgery, brain surgery-related bulbar palsy with laryngeal sensory deficit, bilateral vocal fold palsy detected by LEMG, and history of interventions for the paralyzed vocal fold, such as intracordal injection, laryngeal framework surgery, or laryngoplasty. All aspects of the study were approved by the Human Studies Research Committee of Chang Gung Medical Foundation in accordance with the ethical standards of the 1964 Helsinki declaration. Each participant signed the informed consent before recruitment.

Procedures

In this retrospective study, all participants received quantitative LEMG to confirm the severity of RLN injuries.

Videolaryngostroboscopy, voice acoustic analysis, Voice Outcome Survey (VOS) questionnaire, and Short Form-36 Health Survey (SF-36) quality-of-life questionnaire were assessed within 2 weeks of the day of LEMG. After the baseline assessment, HA injection was performed by the otolaryngologist 2−4 weeks following LEMG examination, if appropriate. Patients who received HA injections also underwent evaluations 1 and 3 months post-injection, including videolaryngostroboscopy, voice acoustic analysis, VOS, and SF-36 questionnaire. All participants enrolled in this study received at least one session of speech therapy.

LEMG examination

Needle LEMG was performed by a board-certified otolaryngologist (T-J.F.) and a physiatrist (Y-C.P.) according to the standard protocol, using a Nicolet Viking Select system (Cardinal Health, Dublin, OH, USA) with a band-pass filter set between 20 Hz and 10 kHz.

Patients were seated on a reclining laryngeal examination chair with an adjustable neck−head rest. Before the procedure, the patient was placed with their neck extended and received a subcutaneous injection of 0.2−1 mL 2% lidocaine hydrochloride at the needle insertion sites. Bilateral TA−LCA muscle complexes and CT muscles were examined using a concentric needle electrode with the surface−ground electrode adhered to the forehead.

The function of the TA−LCA muscle complex was evaluated by getting the patient to produce three series of /e/ vowels at three different intensities (low, moderate, and highest possible), with each /e/ lasting at least 400 ms and each inter-/e/ interval lasting around 200 ms. To evaluate the function of the CT muscle, the patient produced a glissando upward /e/ at normal loudness [10].

For each muscle, we first observed the insertional and spontaneous activities, and then performed semi-quantitative motor unit analysis and recruitment analysis, when the rise time of a motor unit action potential was <0.6 ms, indicating a close proximity to the motor unit. An abnormal LEMG was defined as the existence of spontaneous activities (such as fibrillation, positive sharp wave, or complex repetitive discharge), >30% polyphasia, or decreased interference pattern (reduced, discrete, or no interference pattern). Motor unit recruitment tracings were recorded with sweep speeds of 10 ms per division and a gain of 200 μV per division for off-line analysis.

Hyaluronate intracordal injection

Office-based HA injections [Fig. 1] were performed to relieve UVFP-related symptoms. One session of HA injection was performed for temporary therapy. The neck skin was sterilized with 75% alcohol. A 23-gauge needle was then inserted into the subcutaneous area at the CT junction and approximately 1.0 ml 2% lidocaine hydrochloride was injected. Distal chip fiberoptic laryngoscopy was performed transnasally to observe the vocal cords, and 0.4−1 ml of hyaluronate (Restylane, Q-Med, Sweden; or Juvederm, Allergan, Irvine, CA, USA) was injected into the paralyzed vocal cord. The patient was asked to produce the vowel /e/ at conversational pitch and loudness to allow the change of voice to be monitored during
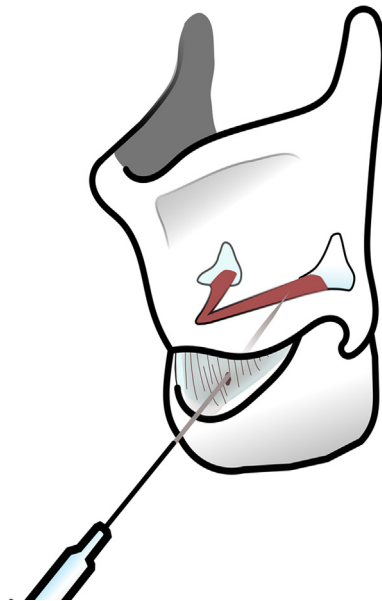

Fig. 1 Office-based intracordal hyaluronate injection guided by transnasal fiberoptic laryngoscope.

HA injection. The injection was stopped when a satisfactory voice was achieved.

Quantitative LEMG analysis

The raw LEMG data were analyzed using Matlab (The Mathworks, Natick, MA, USA). The LEMG waveforms were first binned into non-overlapping epochs, with an epoch duration for the TA−LCA muscle complex of 200 ms [15]. The timing of each turn and its amplitude were computed by the automatic algorithm; specifically, a turn was defined as a change in polarity with an amplitude of at least 100 μV before and after the change, to exclude noise-related peaks. Turn frequency was computed for each epoch as the number of turns divided by the epoch duration, and turn amplitude as the mean of the absolute turn amplitudes. For each muscle, we averaged the turn frequencies for the epochs with turn frequencies that ranked among the top three epochs, to yield the peak turn frequency. The turn ratio was defined as the turn frequency of the lesion-side muscle divided by the turn frequency of the normal-side muscle, to prevent individual bias.

Videolaryngostroboscopy

Each patient was asked to project the vowel /e/ at their habitual pitch and intensity. while sample vocal fold vibrations were recorded by videolaryngostroboscopy. The recording was analyzed offline frame-by-frame using Image J software (Image J 1.44; National Institutes of Health, Bethesda, MD, USA). The normalized glottal gap area (NGGA) was measured from the still image of videolaryngostroboscopy during voicing. The NGGA was computed using the method developed by Omori et al. [16]:

$$NGGA = \frac{\text{Glottal gap area}}{\text{Membranous vocal fold length}^2} \times 100 \text{ units}$$
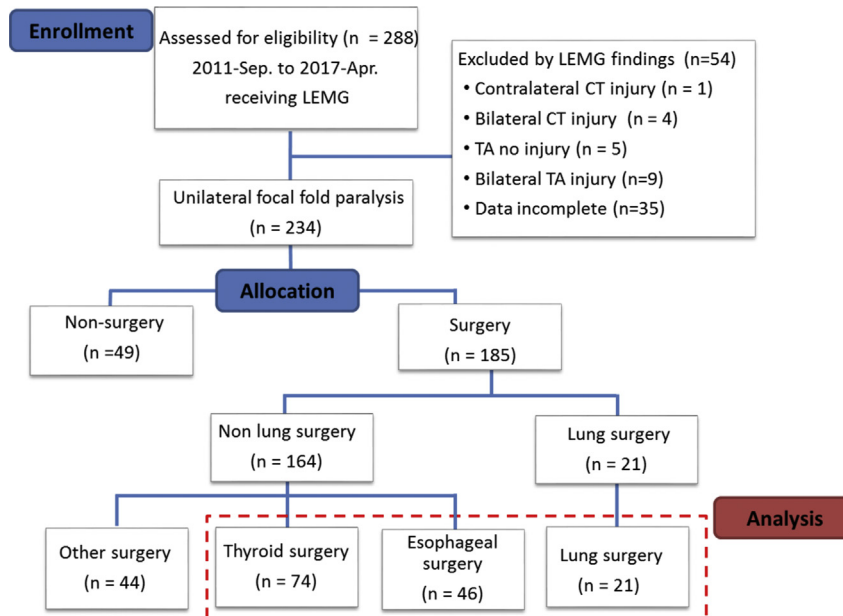
Fig. 2 Flowchart showing patient enrollment, group allocation, and analysis.

The glottal gap area was the image area in square pixels within the glottal area identified using a segmentation process, and membranous vocal fold length was the distance expressed in pixel length from the anterior commissure to the tip of the membranous vocal process. The glottal gap was measured in both the maximally open and closed phases during vocal fold vibration to yield open-phase and closed-phase NGGAs, respectively. The NGGA was significant influenced by the position of paralytic vocal fold. That is, a paralyzed vocal fold fixed at median positions would have a smaller NGGA as compared with those fixed at paramedian or more lateral positions.

Voice acoustic analysis

Voice samples were recorded by a certified speech pathologist while the subject read a standard passage with sustaining a vowel at ordinary conversational pitch and loudness. The duration for which a patient sustained an /a/ was the maximal phonation time. We performed acoustic analysis using a stable segment from the mid-portion of the vowel voice sample. A computerized speech laboratory system (CSL4300B 5.05; Kay-PENTAX, Montvale, NJ, USA) was used to record and analyze the voice and yield parameters of fundamental frequency, jitter (frequency perturbation), shimmer (amplitude perturbation), and harmonic-to-noise ratio. The S/Z ratio (S/Z) was calculated as the ratio of /s/ and /z/ durations when producing each of a sustaining /s/ and /z/ as long as possible, respectively [17].

UVFP-specific quality of life: the VOS questionnaire

Gliklich et al. [18] developed the VOS questionnaire using a Likert scaling technique. The VOS questionnaire assessed the physical and social problems caused by UVFP using a five-item, with total scores between 0 (worst) and 100 (best)

[Supplementary Table S1]. The Mandarin version of VOS was validated [19].

General health: the SF-36 quality-of-life questionnaire

The SF-36 quality-of-life questionnaire is a patient-reported health survey consisting of 36 items, with eight scaled scores representing the weighted sums of the questions in each section. Each component scale is directly transformed into a score of 0—100 on the assumption that each question carries an equal weight, with a lower score indicating greater disability. The recall period for SF-36 is 4 weeks. We adopted the SF-36 Assessment Standard Taiwan version 1 with its Taiwanese norm [20,21].

Statistical analysis

Differences between the lung, esophageal, and thyroid surgery groups were compared using χ^2 or Fisher's exact tests for nominal data (such as sex, lesion side, and CT injury) and ANOVA for numerical data. For patients who received HA injection, repeated measures ANOVA was conducted with three assessment times in the three groups, to compare the changes between assessments over time, with the interaction effect indicating the difference in the changes among the groups. For the analyses of fundamental frequency, sex was included as a covariate to adjust for the sex difference. Only complete data were used for statistical analysis, and subjects with missing data were excluded. The level of significance was defined as $P < 0.05$.

Results

We initially screened 288 patients with a working diagnosis of UVFP observed by laryngoscopy [Fig. 2]. Fifty-four patients

were excluded after LEMG evaluation; five for lack of neurogenic signs of paralysis, 14 for simultaneous contralateral involvement, and 35 for incomplete LEMG data. Among the remaining 234 patients, 185 cases were surgery-related and 49 were non-surgery-related. The 185 surgery-related patients included 21, 46, and 74 with lung, esophageal, and thyroid surgery, respectively. Other surgical etiologies (44 patients) were not discussed in this study.

Demographics

The underlying diagnosis and thoracic surgical procedures are summarized in Supplementary Table S2. Seven patients in the lung surgery group received wedge resection, two received segmentectomy, and 12 received lobectomy [Table 1]. Tumors were the main reason for lung surgery, accounting for 80% (17) of patients, while the remaining had pneumothorax (1 patient, 5%), necrotizing granulomatous inflammation (1 patient, 5%), fibrosis (1 patient, 5%), and negative for malignancy (1 patient, 5%). In those patients, the most common characteristics was mediastinal lymphadenectomy involving the aortopulmonary window (lymph node group 5) or upper and lower paratracheal regions (group 2 or 4), as these regions are mostly approximate to the RLNs. Those who did not receive lymphadenectomy in these regions had advanced tumor size or local adhesion, a property making the surgical approaches more aggressive. The three surgical groups differed in terms of sex ($p < 0.001$), age ($p < 0.05$), paralysis side ($p < 0.001$), eSLN injury ($p < 0.01$), and duration from onset to LEMG exam ($p < 0.001$) [Table 2]. Regarding the lesion side, left dominance was observed in the lung (right/left: 3/18) and esophageal surgery (right/left: 6/40) groups compared with the thyroid surgery group, which showed no side dominance (right/left: 36/38). The incidence of CT muscle involvement was lower in the lung (5%) and esophageal surgery groups (11%) compared with the thyroid surgery group (28%) ($p < 0.05$), indicating that lung and esophageal surgeries were less likely to cause eSLN

Table 1 Disease etiology and surgery type in lung cancer patients.

Category	Number (percentage)
Disease etiology (N = 21)	
Tumor	17 (80%)
Adenocarcinoma	10 (46%)
Squamous cell carcinoma	3 (14%)
Invasive thymoma[a]	1 (5%)
Bronchioloalveolar carcinoma	1 (5%)
Pleomorphic carcinoma	1 (5%)
Lipoma	1 (5%)
Pneumothorax	1 (5%)
Necrotizing granulomatous inflammation	1 (5%)
Fibrosis	1 (5%)
Negative for malignancy	1 (5%)
Surgery type (N = 21)	
Wedge resection	7 (33%)
Segmentectomy	2 (10%)
Lobectomy	12 (57%)

[a] WHO type B3.

injury. The referred interval differed among the three groups ($p < 0.001$), and the thyroid surgery group (3.9 ± 1.9 months) had a longer referred interval than the esophageal surgery group (2.4 ± 1.7 months).

Quantitative LEMG

Quantitative recruitment analysis showed no difference in turn frequency or turn ratio of the TA—LCA muscle complex in the lesion side among the three groups, indicating equal denervation of the RLN. There was also no difference in turn frequency of the TA—LCA muscle complex in the normal side among the three groups [Table 2].

Videolaryngostroboscopy

There was no significant difference in closed-phase ($p = 0.71$) or open-phased NGGA ($p = 0.36$) among the three groups, indicating comparable glottal gaps [Table 2].

Voice acoustic analysis

Among the measured acoustic parameters, only jitter ($p = 0.04$) differed significantly among the three groups. Specifically, the lung surgery group (5.8 ± 5.6) had higher jitter than the esophageal surgery group (5.0 ± 5.0), and the esophageal surgery group had higher jitter than the thyroid surgery group (3.6 ± 2.4). Other voice parameters, including fundamental frequency, maximal phonation time, S/Z ratio, shimmer, and harmonic-to-noise ratio were similar in all three groups [Table 2].

UVFP-related health: VOS questionnaire

There was no difference in VOS score among the three groups [Table 2], indicating comparable voice-related quality of life.

General health: SF-36 questionnaire

Patients in the lung surgery group had similar scores to the other two groups in all SF-36 domains, indicating comparable health-related quality of life. However, the physical functioning ($p < 0.001$) and bodily pain ($p < 0.001$) domain scores differed among the three groups, with the thyroid surgery group having higher scores than the esophageal surgery group [Table 2].

Chronological changes in parameters following HA injection

Eighty-seven patients, including 16, 30, and 41 patients in the lung, esophageal, and thyroid surgery groups, respectively, received HA injection. Time—group analysis showed an interaction effect (3 times × 3 groups) for jitter in acoustic analysis ($p = 0.02$) [Supplementary Table S3]. Specifically, jitter showed the greatest improvement in the lung surgery group (from 6.9 ± 6.2 to 1.6 ± 0.9), compared with the esophageal surgery (5.3 ± 5.6 to 2.7 ± 1.8) and thyroid surgery groups (3.7 ± 2.4 to 2.1 ± 1.5). We observed improvements in all measured patients in the lung surgery group in most parameters of voice acoustic analysis, VOS, and SF-36 ($p < 0.05$),

Table 2 Comparison of parameters among the three study groups.

Parameter	LS group (a)	ES group (b)	TS group (c)	p value	Post-Hoc
Sex (male/female)	10/11	41/5	12/62	<0.001***	ab, bc, ac
Age (years)	62 ± 16.0	55.5 ± 7.1	52.8 ± 14.3	0.02*	ac
Paralysis side (right/left)	3/18	6/40	36/38	<0.001***	bc, ac
eSLN injury (yes/no)	1/20	5/41	21/53	<0.01*	bc, ac
Duration from onset to laryngeal electromyography (months)	3.0 ± 2.2	2.4 ± 1.7	3.9 ± 1.9	<0.001***	bc
Videolaryngostroboscopy	N = 20	N = 44	N = 70		
Closed-phase NGGA	7.9 ± 6.6	9.8 ± 11.4	8.6 ± 9.6	0.71	
Open-phase NGGA	15.2 ± 6.9	18.3 ± 11.7	19.1 ± 11.2	0.36	
Recruitment analysis	N = 21	N = 46	N = 74		
Normal side of TA-LCA (turn/s)	932 ± 275	1015 ± 370	909 ± 305	0.22	
Lesion side of TA-LCA (turn/s)	318 ± 211	379 ± 375	310 ± 253	0.44	
Voice acoustic analysis	N = 21	N = 44	N = 71		
Maximum phonation time (s)	5.5 ± 5.0	5.0 ± 4.1	6.7 ± 5.1	0.14	
SZ ratio	2.9 ± 3.6	2.0 ± 1.1	2.0 ± 1.4	0.16	
Fundamental frequency (Hz)[a]	194 ± 53	148 ± 48	199 ± 64	0.37	
Jitter (%)	5.76 ± 5.59	4.97 ± 5.01	3.55 ± 2.37	0.04*	ab, bc
Shimmer (dB)	0.95 ± 0.96	0.96 ± 0.73	0.86 ± 0.93	0.81	
Harmonic-to-noise ratio	5.71 ± 3.76	5.58 ± 2.96	6.38 ± 2.82	0.34	
Quality of life	N = 19	N = 43	N = 70		
Voice Outcome Survey	42.9 ± 17.8	38.0 ± 20.2	33.4 ± 17.5	0.11	
SF-36					
Physical functioning	74.2 ± 16.3	63.7 ± 24.6	77.6 ± 17.8	<0.001***	bc
Role limitation due to physical health	31.6 ± 43.2	16.9 ± 34.0	35.4 ± 44.1	0.07	
Role limitation due to emotional problem	56.1 ± 38.6	38.0 ± 44.0	50.5 ± 44.2	0.21	
Vitality	56.8 ± 23.3	49.0 ± 19.9	51.1 ± 17.7	0.33	
Mental health	71.8 ± 22.7	64.7 ± 18.8	61.5 ± 18.1	0.11	
Social functioning	61.9 ± 26.5	51.3 ± 26.0	55.1 ± 25.5	0.32	
Bodily pain	78.4 ± 16.5	64.0 ± 25.1	77.7 ± 21.5	<0.001***	bc
General health perceptions	57.1 ± 19.7	48.6 ± 22.7	50.9 ± 22.1	0.38	

LS (a): lung surgery group; ES (b): esophageal surgery group; TS (c): thyroid surgery group.
Data are presented as mean ± standard deviation.
Abbreviations: eSLN: external branch of superior laryngeal nerve; NGGA: normalized glottal gap area; TA-LCA: thyroarytenoid-lateral cricoarytenoid muscle complex.
*$p < 0.05$; ***$p < 0.001$.
[a] p-value adjusted by sex.

except fundamental frequency in acoustic analysis and mental health in SF-36 [Table 3, Fig. 3], indicating that the effect of HA injection was robust and improved clinical presentations across a variety of clinical domains in patients with lung surgery-related UVFP. Among patients in the lung surgery groups, the improvement of measured parameters was greater in the those received HA injections than those received no injection [see Supplementary Fig. S1].

Table 3 Chronological changes in Voice Outcome Survey items following intracordal hyaluronate injection: baseline, and 1 and 3 months follow-up in the lung surgery group.

Score (N = 16)	Baseline	1m post injection	3m post injection	p value
Item 1	34.4 ± 22.1	65.6 ± 15.5	65.6 ± 20.2	<0.001
Item 2	25.0 ± 36.5	59.4 ± 32.8	65.6 ± 35.2	<0.001
Item 3	39.1 ± 25.8	82.8 ± 19.8	82.8 ± 15.1	<0.001
Item 4	50.0 ± 27.4	71.9 ± 27.2	70.3 ± 18.8	<0.05
Item 5	48.4 ± 26.6	75.0 ± 20.4	78.1 ± 15.5	<0.001
Total score	39.4 ± 16.2	70.9 ± 16.5	73.6 ± 14.6	<0.01

Discussion

This study showed that lung surgery-related UVFP had distinct presentations including more left-side involvement, less eSLN injury, and more severe impairments in voice harmonics and frequency control. Given the unique location and length, the left RLN is more frequently injured during surgical procedures among patients with thoracic diseases [22]. Accordingly, lung surgery patients in the current study has a higher proportion of left-RLN injuries (83%), while has an almost negligible chance of causing eSLN lesions, though eSLN injuries are conversely quite common in thyroid surgery [12].

The left RLN has substantial risk of injury during left-sided cardiothoracic interventions. An important finding of this study is that most patients received lymphadenectomy on lymph node groups approximate to the RLN (groups 5, 2, and 4) and remaining patients had large lesions, such as large tumors, or had lesions complicated with adhesion, indicating that these characteristics could be the risk factors for RLN injuries. To prevent this type of injury, Zhao et al. applied intraoperative RLN monitoring during left lung surgery, with
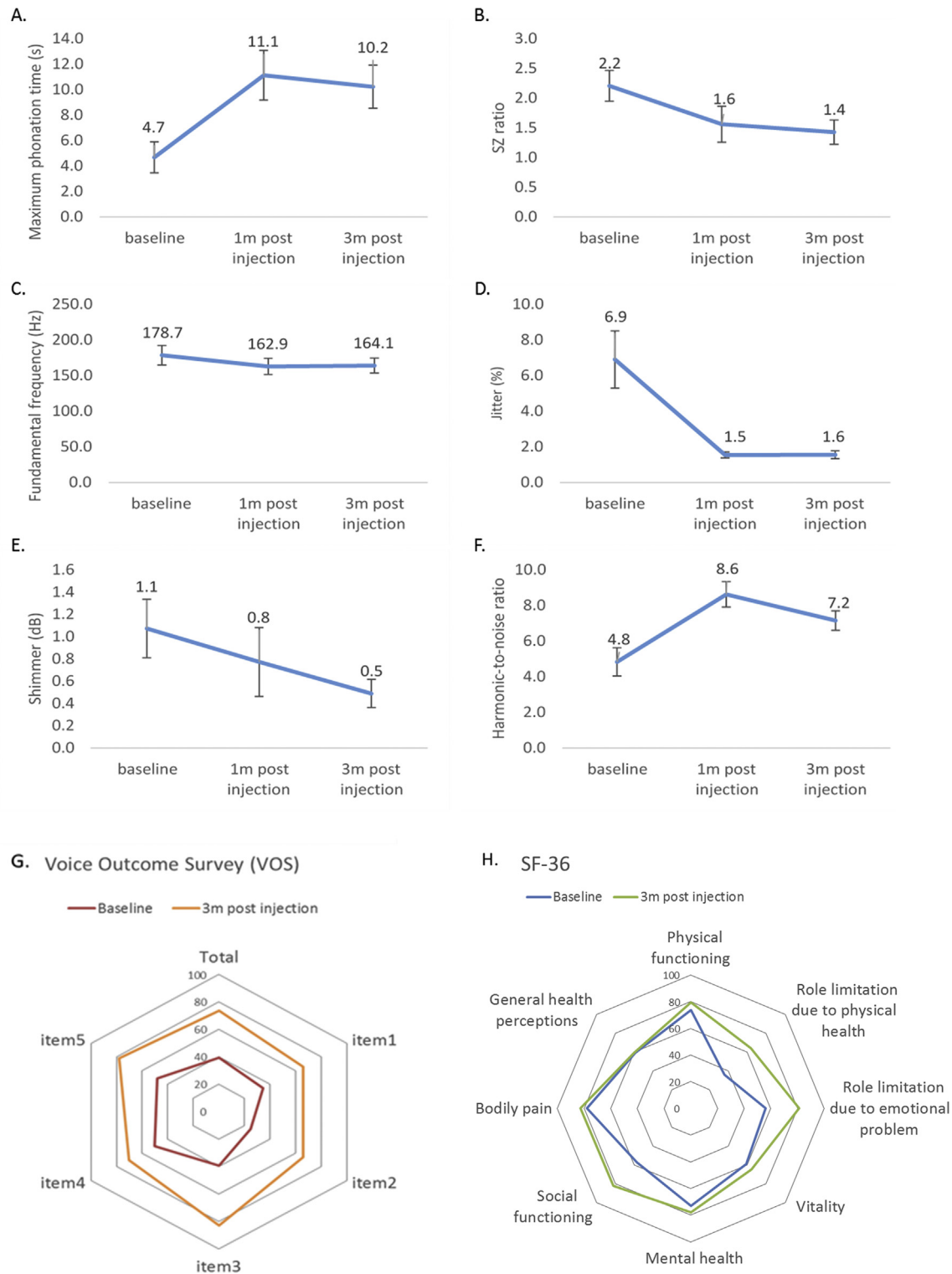
Fig. 3 Chronological changes in voice acoustic analysis, Voice Outcome Survey (VOS), and Short Form-36 Health Survey (SF-36) at baseline and at 1 and 3 months post-hyaluronate injection in the lung surgery group. (A) Maximal phonation time, (B) SZ ratio, (C) fundamental frequency, (D) jitter, (E) shimmer, (F) harmonic-to-noise ratio, (G) VOS item scores (items 1—5) and total score. (H) SF-36 domain scores.

good efficacy for indentifying the RLN in the surgical side. However, it is still uncommon in monitoring RLNs during lung surgery [11].

Lung surgery-related UVPF has distinct pathophysiological mechanisms that further impede patient recovery and make the dysphonia more profound. Patients undergoing

thoracic surgery usually have a smoking history, manifesting with chronic obstructive pulmonary disease and poor pulmonary function [23]. Aging also decreases the compliance of the chest wall and respiratory muscle strength, and changes the surfactant composition [24], further affecting the respiratory force responsible for driving voice production. The vital capacity and forced expiratory volume in 1 s decrease significantly in the early phase post-lung resection. This decline partially recovers over the following months [25], but does not recover to its preoperative level [14]. Importantly, Iwarsson et al. reported that limited lung volume in these patients decreased the airflow, thus affecting phonation [26]. Voice rehabilitation training implemented either preoperatively or post-operatively may thus improve lung function, decrease pulmonary complications, and shorten postoperative hospital stay [27,28].

Early interventions have been reported to benefit patients with a variety of surgery-related UVFPs [29]. Specifically, laryngeal medialization for UVFP caused by thoracic surgery with mediastinal dissection has great benefits on swallowing, speech and voice [30]. Recent developments in office-based injection laryngoplasty have enabled patients referred early to an otolaryngologist to undergo HA injection, providing immediate voice restoration and long-lasting improvements in quality of life [13]. Indeed, office-based HA injection does not need general anesthesia or sedation so that it is safer. Importantly, the results of this study demonstrated that HA injection dramatically improved the functional and quality-of-life across surgery types. Early referral is recommended especially for patients with post-lung-surgery hoarseness with risk factors with prolonged denervation, such as lymphadenectomy approximate to the RLN. Indeed, patients post-lung surgery suffered an immediate reduction in pulmonary function [25], and had difficulty to receive other major operations. Office-based HA injection restored the control of subglottal pressure and thus improved jitter and voice quality.

This study had some limitations. First, there were sex differences among the three groups, which may have resulted in bias in terms of the observed results of voice acoustic analysis. Second, the lung surgery group was smaller than the other two groups. A case series with a large sample size is therefore needed to analyze the differences in UVFP across different lung disease etiologies and/or different surgery types.

Conclusions

Lung surgery-related UVFP is characterized by a higher frequency of left-side involvement, a lower proportion of eSLN injuries, and more severe impairments in voice harmonics and frequency control. Following office-based HA injection, lung surgery-related UVFP showed the greatest improvement in jitter. These findings indicate that lung surgery-related UVFP is a distinct type of UVFP, and that early intervention, such as office-based HA injection, is recommended to facilitate recovery of the patient's voice and psychosocial functions.

Ethics approval and consent to participate

Funding

Conflicts of interest

Acknowledgments

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.bj.2020.07.005.

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