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Impact of patient-related factors on successful autologous fat injection laryngoplasty in thyroid surgical treated related unilateral vocal fold paralysis- observational study

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Abstract

The aim of this study was to compare major voice indicators in different sub-categories, the outcome of lipoinjection for patients might be refined and some voice prognostic factors could be more particularized in specific sub-groups. This is an observational study, and sub-grouped UVFP patients into 3 categories: male vs female, BMI ≥ 24 vs BMI < 24, Age ≥ 60 vs Age < 60 for more detailed exploring whether sub-categories affected voice diagnostic and prognostic parameters. Patients' voice data is recorded before and after the autologous fat injection laryngoplasty by a multidimensional voice program. Overall, 73 patients' voice performance were improved 12 months later by vocal fold lipoinjection. In the comparison of the male with female revealed female obtained better Jita than male by surgery (Female: 174.50 ± 100.58 Hz; Male: 294.82 ± 253.65 Hz; $P < .05$). BMI ≥ 24 vs BMI < 24 showed no statistical difference. Patients aged under 60 demonstrated better Highest F0, lowest F0, NHR and ShdB than elder ones 12 months after receiving vocal fold lipoinjection. Thus, Noise-to-harmonics ratio (NHR), voice turbulence index (VTI), and ShdB (Absolute shimmer, dB) may be the major post-operative evaluating markers of patients' age under 60. Voice parameters showed no significant correlation with BMI. Female patients performed lower Jita (Absolute jitter, μsec) than male patients 1 year after receiving treatment. The experimental results in this study showed UVFP patients' gender and age may stand as significant categories on analyzing clinical voice prognostic indicators, ShdB and Jita of autologous injection laryngoplasty.

Abbreviations: BMI = body mass index, GRBAS = grade, roughness, breathiness, asthenia, and strain, MDVP = stroboscopy examination, and multidimensional voice program, MPT = max phonation time, NHR = noise-to-harmonic ratio, OP = operation, SERF = stroboscopy examination rating form, SPI = soft phonation index, UVFP = unilateral vocal fold paralysis, VHI-10 = voice handicap index-10, VTI = voice turbulence index.

Keywords: autologous injection laryngoplasty, unilateral vocal fold paralysis, voice performance

1. Introduction

Symptoms of voice disorders are also called dysphonia, which indicates abnormal frequency or amplitude during vocal fold vibration. The clinical manifestation is hoarseness, breathiness, roughness and tenseness of voice.[1] One of the main causes of voice disorder could be glottic insufficiency, which is caused by the imperfect closure of the vocal folds. Etiologies of incomplete closure of the vocal folds include neuromuscular paralysis, scarring, atrophy, or sulcus vocalis. The common and reliable clinical diagnostic of glottic insufficiency is the laryngostroboscopic examination, which is able to reveal and record the appearance and movement of vocal fold.[2]

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Current interventions in treating glottic insufficiency of the vocal fold are either by laryngeal framework surgery or by injection augmentation. With the advanced clinical approach, vocal fold injection may become a major mode of treatment for dysphonia patients.[3] Among various vocal fold injection treatments, autologous fat is one of the safe and reliable injection options.[4] However, a small amount of unilateral vocal fold paralysis (UVFP) patients received poor outcomes after receiving lipoinjection surgery.[5]

In this study, patients with vocal cord paralysis caused by thyroid surgery were given an autologous fat injection. There were subjective and objective human vocal measurements which include grade, roughness, breathiness, asthenia, and strain (GRBAS) scale, voice handicap index-10 (VHI-10) questionnaires, max phonation time (MPT), stroboscopy examination, and multidimensional voice program (MDVP).[6] We recorded and analyzed several voice quality indicators, such as highest F0, lowest F0, Jita (frequency perturbation, absolute jitter, Hz), ShdB (perturbation of amplitude, absolute shimmer, dB), voice turbulence index (VTI), soft phonation index (SPI) and noise-to-harmonic ratio (NHR) before and one year after autologous fat injection.[7,8] The voice quality indicators can be of clinical diagnostic assistance, and can help otolaryngologists to determine the best strategy for UVFP patients.

Autologous fat injection laryngoplasty is an useful early salvage for patients with thyroid related iatrogenic UVFP and could mostly help patient to have better voice quality. However, the voice quality is unpredictable and affect patients' speech function and even affect the patient's emotion, this also bothers the clinicians when picking this method for patient with UVFP after thyroid surgery. Therefore, we raise this study for clinicians and patients for doctor's making proper treatment strategies and for patient's preferences for getting the better treatment outcome when treating UVFP. Patients with thyroid related iatrogenic UVFP in different gender, BMI and age produced different voice quality outcomes after fat injection laryngoplasty. The goal of this study is to find out gender, age, and BMI influence what voice parameters by fat injection laryngoplasty in longer term voice quality survey. Konomi et al previously suggested that gender affects voice outcome in UVFP patients underwent arytenoid adduction and medialization thyroplasty. Male patients showed significant extension of post-pitch range whereas female showed no significant difference in pitch range after surgery. They assumed it may be caused by operative effects of smaller larynx among female patients.[9] In addition, Li et al divided and analyzed UVFP patients into 4 age groups including Group A enrolled patients with an age less than 30 years; Group B, 30 to 44 years; Group C, 45 to 59 years; Group D, ≥60 years. Moreover, their results assumed age could be a surgical outcome in laryngeal reinnervation for UVFP patients.[10] Barry et al investigated effect of increased body mass index (BMI) on complication rates during laryngotracheal surgery among 126 patients with different BMI groups (BMI of <25, 25–35, and 36–45).[11] However, age, gender and BMI effects in fat injection laryngoplasty is rarely reported. The definition of thin and small body weight is 24 and patients with BMI less than 24 usually with hardly fat harvested compare to BMI over 24, therefore we use 24 as cut off point for low body weight. Elder patient is considered with poor fat content and quality of fat is not as good as younger patients, and we just want to survey whether is age an important risk factor.

Therefore, this study is to evaluate the outcome of lipoinjection in different sub-categories and to determine the suitable parameters for prognostic purpose. Thus, these three sub-categories, that is, male vs female, body mass index (BMI) ≥ 24 vs BMI < 24, and Age ≥ 60 vs Age < 60, were analyzed to determine their effect on voice diagnostic and prognostic parameters.

Table 1

Demographic characteristics of total UVFP patients.

Item	Patients (n = 73)
Age (yr)	54.71 ± 12.55
Gender (Male/Female)	36/37
BMI	22.38 ± 4.01
GRBAS (pre-op)	
Grade	2.41 ± 0.55
Roughness	2.32 ± 0.63
Breathiness	2.21 ± 0.7
Asthenia	2.32 ± 0.8
Strain	2.06 ± 0.75
Stroboscopy examination rating form Anterior-posterior	2.64 ± 0.65
Left-right	2.61 ± 0.66
Voice handicap index - 10 (sum)	29.96 ± 4.63

BMI = body mass index, GRBAS = grade, roughness, breathiness, asthenia, and strain, UVFP = unilateral vocal fold paralysis.

2. Material and methods

2.1. Subjects

Between March 2012 and February 2015, 73 patients with UVFP in China Medical University Hospital provided informed consent before lipoinjection laryngoplasty and the Institutional Review Board of the hospital approved the research. Among 73 UVFP patients, there are 36 male and 37 female patients, the average age was 54.71 ± 12.55 years old as shown in the Table 1. Successfully treated groups were defined as having significant improvement on MPT and were defined as reaching to 30% increase rate with improvement of GRBAS scale after 1 year injection laryngoplasty determined by one laryngologist. We compared pre- and post-treated voice parameters, gender, BMI, and age before injection laryngoplasty to survey predictors for this surgery.

2.2. Assessments

Six criteria in this study are the basis of evaluations of UVFP: MPT, GRBAS scale, VHI-10, MDVP computerized voice record analysis, laryngostroboscope assurance, and the lack of laryngeal electromyography responses (spontaneous fibrillation activity with minimal recruitment on voluntary action) in the unilateral thyroarytenoid muscle. The assessments were performed by an otolaryngologist. Following an observation period of 1 year, all patients underwent autologous fat injection laryngoplasty for their dysphonia problems. One year after lipoinjection surgery, UVFP patients were called back to the hospital and received the MDVP voice record and laryngoscope diagnostic for prognosis assessment.

2.3. Acoustic analysis

The MPT was recorded while UVFP patients were told to take a deep breath and pronounce the vowel /a/ with the microphone as long as possible. At the same time, a 5-second voice recording was collected and several voice parameters such as Jita (absolute jitter, Hz), ShdB (shimmer in dB), NHR, VTI and SPI were analyzed by the MDPV program (Computerized Speech Lab, Kay Pentax 4500). All these acoustic assessments were approved to proceed

in the ENT of China Medical University Hospital, and were performed by a speech therapist.

2.4. Clinical evaluation

The GRBAS, VHI, videostroboscopy, and laryngeal EMG were used for clinical evaluation by the otolaryngologist.

(1) GRBAS is a clinical acoustic evaluated questionnaire which renders the grade of hoarseness; Roughness, Breathiness, Asthenia, and Strain from scores of 0, 1, 2, or 3, where 0 is normal, 1 is a mild degree, 2 is a moderate degree, and 3 is a severe degree of hoarseness.
(2) The VHI-10 was another clinical voice assessed questionnaire in which otolaryngologist gave 10 questions to patients as shown below:
   (a) My voice makes it difficult for people to hear me
   (b) I run out of air when I talk.
   (c) People have difficulty understanding me in a noisy room.
   (d) The sound of my voice varies throughout the day.
   (e) My family has difficulty hearing me when I call them
   (f) I use the phone less often than I would like to.
   (g) I'm tense when talking to others because of my voice.
   (h) I tend to avoid groups of people because of my voice.
   (i) People seem irritated with my voice.
   (j) People ask, "What's wrong with your voice?"
(3) Each question corresponds to its scores (from 0 to 4) in which 0 means never, 1 means almost never, 2 means sometimes, 3 means almost always, and 4 means always.
(4) The stroboscopy examination rating form (SERF) was a reliable assessment to evaluate the supraglottic closure with videostroboscopy. By measuring distances of front and rear and left and right of the glottis, SERF was scored from 0 to 4 in which 0 is normal; 1 is slight imperfect closure; 2 is medium imperfect closure; 3 is severe imperfect closure; 4 means glottis cannot be closed[12]
(5) The UVFP patients were also examined through laryngeal electromyography (EMG) after acoustic examination. EMG was a stable technique performed to assess the physiological activity of the muscle. For the purpose of diagnosing laryngeal movement disorders, the Laryngeal EMG could examine electrical activity of thyroarytenoid and LCA muscles that were tested, as well as electrical activity as patients phonated vowel /a/.

2.5. Autologous fat injection laryngoplasty

The periumbilical subcutaneous area was the source of autologous fat for injection laryngoplasty. The surgical procedure of obtaining autologous fat is shown below. First of all, a local infiltration 0.5 cm beneath the umbilical area incision was made. A physician injected the mixed solution between 30 and 50 ml into the periumbilical subcutaneous area to elute fat for 5 minutes. The formula of the fat-elution solution was: Lidocaine hydrochloride (20 ml), dexamethasone (1 ml), 7% sodium bicarbonate (20 ml), and epinephrine (5 mg) were added to 500 ml of sodium chloride. Secondly, a 10-ml Storz injection syringe (Karl Storz, Tuttlingen, Germany) was used to harvest fat globules. Using the several steps described above, 30 to 40 ml of subcutaneous adipose soft tissue was harvested, then washed with a normal saline solution to remove blood clots and rinsed in (10 ml) of regular insulin for 5 minutes. Finally, the target area which was located at the posterior third of the membranous vocal fold, on the lateral aspect of the thyroarytenoid muscle was injected with fat with the syringe under general anesthesia. Otolaryngologist injected the fat into the paralyzed site until 20% to 30% bulging across the midline of vocal fold (Fig. 1).

2.6. Statistical analysis

The data were analyzed by SPSS 21 software (SPSS Inc., Chicago, IL). Descriptive statistics was used to analyze the continuous

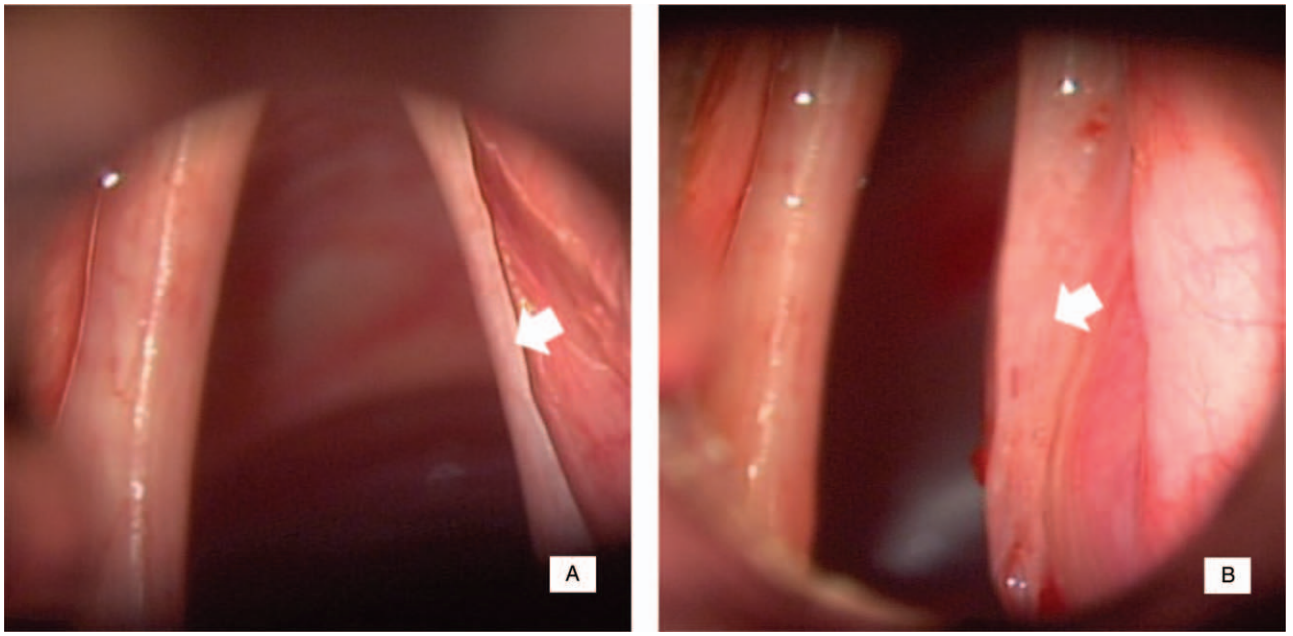

Figure 1. Autologous fat injection laryngoplasty: before (A) and after (B) autologous injection.

Table 2

Outcomes before and after autologous fat injection laryngoplasty (n = 73).

Items	Pre-op	Post-op	Improved	*P* value
MPT (sec.)	5.95 ± 4.15	8.77 ± 4.92	+	.02*
GRBAS sum	10.55 ± 1.40	8.10 ± 2.33		.01*
Grade	2.41 ± 0.55	1.50 ± 0.71	+	.002*
Roughness	2.32 ± 0.63	1.30 ± 0.48	+	.001*
Breathiness	2.21 ± 0.71	1.60 ± 0.70	+	.02*
Asthenia	2.32 ± 0.82	1.80 ± 0.42	+	.004*
Strain	2.06 ± 0.75	1.90 ± 0.57	+	.44
Stroboscopy rating form				
Anterior-posterior	2.64 ± 0.65	1.18 ± 0.44	+	2.07
Left-right	2.61 ± 0.66	1.11 ± 0.33	+	4.89
Voice handicap index-10 (sum)	29.97 ± 2.15	23.80 ± 5.77	+	1.85
MDVP analysis				
Highest F0 (Hz)	245.37 ± 106.20	243.51 ± 114.44	+	.92
Lowest F0 (Hz)	151.48 ± 55.40	133.47 ± 46.90	+	.04*
NHR	0.28 ± 0.42	0.22 ± 0.17	+	.29
VTI	0.07 ± 0.07	0.07 ± 0.09	–	.88
SPI	21.84 ± 17.03	21.47 ± 17.45	+	.9
Jita (μsec.)	311.75 ± 380.45	232.89 ± 198.83	+	.13
ShdB (dB)	0.81 ± 0.70	0.78 ± 0.58	+	.77

* $P < .05$.

+ = improved after receiving surgery, MPT = max phonation time, Jita = absolute jitter, NHR = noise-to-harmonic ratio, ShdB = shimmer in dB, SPI = soft phonation index, VTI = voice turbulence index.

variables, and was represented as means and standard deviations. The statistical data of MPT, GRBAS, stroboscopy rating form, voice handicap index-10, and MDVP analysis were performed by Shapiro-Wilk test, showing normal sample distribution. The data pre- and post- autologous injection laryngoplasty were compared by paired-t test. The t test was used to analyze and compare the parameters, that is, MPT, GRBAS, SERF, VHI-10, and MDVP before and after autologous injection laryngoplasty. Then those parameters were compared between under 3 categories: male vs female, BMI ≥ 24 vs BMI < 24, and Age ≥ 60 vs Age < 60. The level of significance was set at $\alpha < 0.05$, and two tailed test was used.

3. Results

3.1. Comparing all patients' voice quality 1 year after lipoinjection: MPT, GRBAS, lowest F0 showed the statistical differences

Seventy-three UVFP patients received MDVP voice record analysis before and after lipoinjection. All patients' demographic characteristics are shown in Table 1. All patients were asked to pronounce the vowel /a/ as stable as possible. While recording the voice quality, several parameters were obtained and analyzed by the MDVP computer program. Then, voice quality parameters were compared pre and post operation. All voice diagnostic parameters include MPT, GRBAS, stroboscopy examination rating form, VHI, Highest F0, lowest F0, NHR, SPI, Jita, ShdB, except VTI present improved vocal quality within all cases after receiving lipoinjection surgery (Table 2).

MPT, GRBAS, lowest F0 showed significant differences 12 months after the clinical operation. Before the injection laryngoplasty, the average of 73 patients' MPT (max phonation time) was the 5.95 ± 4.15 s, 1 year after lipoinjection, the average of 73 patients' MPT became 8.77 ± 4.92 s, which showed significance ($P < .05$) in the voice improvement of MPT after injection laryngoplasty. Furthermore, GRBAS scores also present statistical significance ($P < .05$) before and after surgery. The summation GRBAS scores were 10.55 ± 1.40 before surgery which decreased to 8.10 ± 2.33 1 year after lipoinjection. In Table 2, lowest F0 is also another voice diagnostic indicator showed the statistical difference before and after surgery (pre-op: 151.48 ± 55.40 Hz, post-op: 133.47 ± 46.90 Hz; $P < .05$).

3.2. Comparing prognosis of lipoinjection between male and female groups

Patients of different gender may demonstrate different surgical outcomes. Thus, the patients were divided into 2 groups (37 female and 36 male), and analyzed the prognosis of lipoinjection (Table 3). There were no significant differences on the parameters, i.e. MPT, GRBAS, SERF, VHI-10, and MDVP, before and after lipoinjection between the 2 groups. Jita (Absolute Jitter, μs), which is an important vocal fold short-term frequency control, likewise showed the statistical difference between male and female (male: 294.82 ± 253.65 μsec.; Female: 174.50 ± 100.58 μs; $P < .05$; Table 3).

3.3. Comparing prognosis of lipoinjection between patients' BMI ≥ 24 and BMI < 24

We also surveyed whether BMI is another prognostic factor for injection laryngoplasty. According to WHO, increased risk of overweight among Asian BMI group were identified as 23 kg/m^2 or higher[13] and, therefore, we divided all these 73 patients into BMI ≥ 24 or BMI < 24. However, there is no statistical difference in all parameters before and after lipoinjection between these 2 groups (Table 4).

3.4. Comparing prognosis of lipoinjection between patients' age ≥ 60 and age < 60

The acoustic analysis revealed a statistical difference in voice performance following vocal fold lipoinjection by age (Table 5).

Table 3

Comparison of all parameters between male and female.

Items	Male (n = 36)		Female (n = 37)	
	Pre-OP	Post-OP	Pre-OP	Post-OP
MPT (s)	6.24 ± 5.35	10.70 ± 6.94*	5.11 ± 2.55	7.17 ± 1.72*
GRBAS sum	11.35 ± 0.73	7.50 ± 2.08*	11.20 ± 0.57	8.50 ± 2.59*
Grade	2.45 ± 0.56	1.25 ± 0.50*	2.35 ± 0.54	1.67 ± 0.82*
Roughness	2.39 ± 0.66	1.25 ± 0.50*	2.24 ± 0.61	1.33 ± 0.52*
Breathiness	2.27 ± 0.76	1.50 ± 0.58	2.12 ± 0.64	1.67 ± 0.82
Asthenia	2.27 ± 0.80	1.75 ± 0.50	2.35 ± 0.81	1.83 ± 0.41
Strain	2.00 ± 0.71	1.75 ± 0.50	2.09 ± 0.79	2.00 ± 0.63
Stroboscopy rating form				
Anterior-posterior	2.70 ± 0.65	1.25 ± 0.50*	2.55 ± 0.62	1.13 ± 0.44*
Left-right	2.63 ± 0.67	1.00 ± 0.01*	2.55 ± 0.62	1.13 ± 0.44*
Voice handicap	15.13 ± 1.07	24.00 ± 3.10*	14.73 ± 1.01	24.00 ± 3.10*
index-10 (sum) MDVP analysis				
Highest F0 (Hz)	229.76 ± 141.03	240.78 ± 120.12	259.65 ± 57.60	245.87 ± 110.89
Lowest F0 (Hz)	175.99 ± 51.58	132.44 ± 40.57	174.79 ± 48.60	134.23 ± 50.13
NHR	0.38 ± 0.57	0.24 ± 0.18	0.19 ± 0.15	0.21 ± 0.16
VTI	0.08 ± 0.06	0.08 ± 0.10	0.07 ± 0.07	0.07 ± 0.07
SPI	22.77 ± 19.64	25.37 ± 22.07	21.00 ± 14.48	17.80 ± 10.62
Jita (μs)	318.43 ± 267.81	294.82 ± 253.65	214.22 ± 246.85	174.50 ± 100.58†
ShdB (dB)	0.96 ± 0.73	0.92 ± 0.67	0.68 ± 0.65	0.65 ± 0.46

Jita = absolute jitter, MPT = max phonation time, NHR = noise-to-harmonic ratio, OP = operation, ShdB = shimmer in dB, SPI = soft phonation index, VTI = voice turbulence index.
* Pre- vs post-OP, $P < .05$.
† Male vs female, $P < .05$.

Comparing between the 2 groups, the parameters before lipoinjection did not have significant differences. There were significant differences in highest F0, lowest F0, NHR, VTI, SPI, ShdB, between age ≥60 and age <60 (Table 5). With respect to exquisite assessment of vocal fold control, we found age under 60 exhibited better NHR (Age ≥ 60: 0.28 ± 0.16; Age < 60: 0.19 ± 0.16; $P < .05$) and ShdB (Age ≥ 60: 1.05 ± 0.63 dB; Age < 60: 0.63 ± 0.50 dB; $P < .001$) by receiving vocal fold lipoinjection after 12 months (Table 5). Overall, there were improvement of MPT and GRBAS scales by gender, BMI and age after autologous fat injection laryngoplasty and the results were showed in Figures 2 and 3.

4. Discussion

The statistical results of 73 UVFP patients who underwent lipoinjection surgery 1 year later revealed the MPT and lowest F0, which means the lowest fundamental frequency, had the most

Table 4

Comparison of all parameters between BMI ≧ 24 and BMI < 24.

Items	BMI ≧ 24		BMI < 24	
(n = 45)	(n = 28)	Post-OP	Pre-OP	Post-OP
MPT (s)	4.66 ± 2.95	8.00 ± 2.83	6.96 ± 4.97	13.67 ± 7.77
GRBAS sum	10.78 ± 0.72	8.50 ± 2.12	11.12 ± 0.74	7.33 ± 2.52
Grade	2.33 ± 0.50	1.50 ± 0.71	2.38 ± 0.57	1.33 ± 0.58*
Roughness	2.33 ± 0.50	1.50 ± 0.71	2.19 ± 0.75	1.33 ± 0.58
Breathiness	2.00 ± 0.87	1.50 ± 0.71	2.15 ± 0.73	1.33 ± 0.58
Asthenia	2.11 ± 0.93	2.00 ± 0.00	2.31 ± 0.84	1.67 ± 0.58
Strain	2.11 ± 0.93	2.00 ± 0.00	2.00 ± 0.85	1.67 ± 0.58
Stroboscopy rating form				
Anterior-posterior	2.75 ± 0.71	0.88 ± 0.18*	2.52 ± 0.65	1.33 ± 0.58*
Left-right	2.63 ± 0.74	0.88 ± 0.18*	2.48 ± 0.65	1.00 ± 0.22*
Voice handicap index-10 (sum)	15.63 ± 1.41	23.00 ± 1.41*	14.72 ± 1.06	26.00 ± 6.93
MDVP analysis				
Highest F0 (Hz)	247.21 ± 79.62	227.68 ± 102.25	262.13 ± 147.11	261.48 ± 150.22
Lowest F0 (Hz)	123.96 ± 48.57	119.08 ± 48.85	157.51 ± 54.82	131.63 ± 48.57
NHR	0.24 ± 0.21	0.25 ± 0.19	0.36 ± 0.64	0.22 ± 0.18
VTI	0.06 ± 0.06	0.06 ± 0.03	0.06 ± 0.06	0.07 ± 0.07
SPI	23.01 ± 15.11	24.75 ± 18.43	24.95 ± 21.51	25.57 ± 23.07
Jita (μs)	347.97 ± 385.92	266.36 ± 204.98	330.14 ± 508.60	232.42 ± 178.15
ShdB (dB)	0.81 ± 0.63	0.93 ± 0.71	0.86 ± 0.74	0.75 ± 0.55

Jita = absolute jitter, MPT = max phonation time, NHR = noise-to-harmonic ratio, OP = operation, ShdB = shimmer in dB, SPI = soft phonation index, VTI = voice turbulence index.
* Pre- vs post-OP, $P < .05$.

Table 5

Comparison of all parameters between age ≧60 and age <60.

Items	Age < 60 (n=47)		Age≧ 60 (n=26)	
	Pre-OP	Post-OP	Pre-OP	Post-OP
MPT (s)	4.45±3.73	10.13±6.98*	6.19±4.23	8.47±3.43
GRBAS sum	11.53±0.61	7.33±2.52*	10.52±0.68	7.12±2.09
Grade	2.58±0.50	1.33±0.58*	2.30±0.55	1.57±0.79*
Roughness	2.50±0.59	1.33±0.58*	2.20±0.63	1.29±0.49*
Breathiness	2.50±0.59	1.33±0.58*	2.02±0.70	1.71±0.76
Asthenia	2.54±0.72	1.67±0.58*	2.18±0.81	1.86±0.38
Strain	2.42±0.72	1.67±0.58	1.86±0.70	2.00±0.58
Stroboscopy rating form				
Anterior-posterior	2.87±0.63	0.92±0.14*	2.54±0.67	1.29±0.49*
Left-right	2.62±0.63	0.86±0.24*	2.49±0.68	1.14±0.38*
Voice handicap	14.87±0.87	20.50±5.74*	15.00±1.20	24.56±2.81*,†
index-10 (sum) MDVP analysis				
Highest F0 (Hz)	265.75±86.87	289.68±134.48	235.98±114.39	216.67±92.47†
Lowest F0 (Hz)	143.45±55.48	117.39±46.73	157.08±55.35	142.82±44.92†
NHR	0.42±0.63	0.28±0.16	0.20±0.19	0.19±0.16†
VTI	0.10±0.07	0.11±0.12	0.06±0.05	0.06±0.04†
SPI	15.52±14.04	18.03±21.30	24.97±17.66	23.47±14.66
Jita (μs)	307.61±355.36	286.32±255.10	279.92±389.78	201.83±152.29
ShdB (dB)	1.03±0.79	1.05±0.63	0.69±0.61	0.63±0.50†

Jita=absolute jitter, MPT = max phonation time, NHR=noise-to-harmonic ratio, OP=operation, ShdB=shimmer in dB, SPI=soft phonation index, VTI=voice turbulence index.

* Pre- vs post-OP, $P<.05$.

† Age ≧ 60 vs Age < 60, $P<.05$.

Jita=absolute jitter, MPT = max phonation time, NHR=noise-to-harmonic ratio, OP=operation, ShdB=shimmer in dB, SPI=soft phonation index, VTI=voice turbulence index.

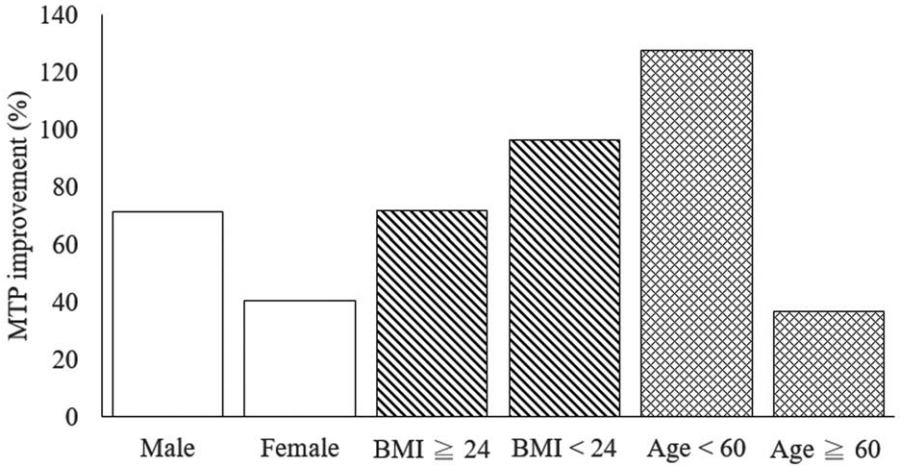

Figure 2. Improvement of max phonation time percentage by gender, age and body mass index after autologous fat injection laryngoplasty.

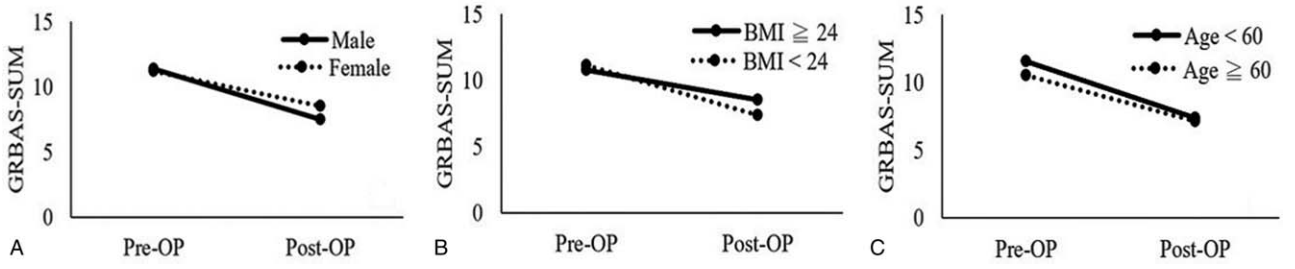

Figure 3. The change of grade, roughness, breathiness, asthenia, and strain-sum percentage by gender (A), age (B) and body mass index (C) before and after autologous fat injection laryngoplasty.

prominent progress among all the other voice quality parameters by MDVP. The fundamental frequency could be probably the most important indicator in speech synthesis and processing, which is formed by the tension of vocal fold cover. Children's vocal folds are smaller and thinner resulting in higher average fundamental frequency (male: 250 Hz, female: 300 Hz). The adult human vocal folds become longer, larger and thicker thus making fundamental frequency lower (male: 80–150 Hz, female: 180–250 Hz).[14] In normal conditions, people could easily adjust higher or lower F0 by changing vocal fold vibration frequency. Higher fundamental frequency would enlarge the harmonic spacing and make the amplitude lower, which means weaker strength. Consequently, lower fundamental frequencies processed stronger voice amplitude energy.[15] In general, this study revealed that patients performed improved MPT and lowest F0 with statistical significance 1 year after lipoinjection surgery.

Our findings in this research also revealed that the female UVFP patients performed significantly lower Jita 1 year after receiving lipoinjection surgery in the gender-divided group. Jita (Absolute Jitter) is an indicator evaluating the period-to-period variability of the pitch period within the analyzed voice sample, and can be interpreted as measureable frequency perturbation.[16] Hence, Jita can be an important voice quality parameter in Otolaryngologists' clinical assessment.[17] The findings of Brockmann et al showed that different gender of healthy subjects had significant effects either on jitter or on shimmer, and it confirmed the results of ours. Men showed significantly less shimmer and higher jitter while decreasing voice loudness in phonations below 75 dB and 80 dB.[18,19] Another team discovered that women were prone to be diagnosed with dysphonia.[20] The results of our work suggested that female UVFP patients recovered lower Jita by surgery and Jita could be a major post-lipoinjection evaluating parameter within female UVFP patients.

Our finding indicated that there is no statistical significance of voice improvement between UVFP patients' BMI under and over 24 after lipoinjection ($P > .05$, Table 4), which is in agreement with the study conducted by Duke et al.[21] The results of Duke et al was also showed that there was no significant difference with complications between patients with a normal BMI and higher BMI. Tamura et al gave another point of view by using a different fat source for the autologous fat surgery.[22] They suggested to otolaryngologists, while facing the insufficient fat source of BMI of vocal fold paralysis patients' lower abdomen as practiced in plastic surgery, that the buccal fat pad could be substitute fat source. Buccal fat cells were relatively smaller and showed continuous effects that were even slightly higher than the abdomen fat.[22,23] Nevertheless, our study showed UVFP patients' BMI (BMI $\geq$ 24 vs BMI $<$ 24) did not affect voice quality after surgery.

Aging could be considered as another key factor that influences post-treatment outcome of voice.[24–26] When comparing two sub-groups of UVFP patients (age $\geq$ 60 and age $<$ 60), the younger generation performed better vocal progress in highest F0, lowest F0, NHR, VTI, and ShdB in this study. The improvement of VTI and NHR stands for the decrease of the ratio of inharmonic spectral energy to spectral harmonic energy. This means younger patients' (age $<$ 60) voices tend to be clearer and quieter than older patients, (age $\geq$ 60) after receiving the treatment, and our result was the same as the previous study of Bhuta et al.[27] Lin et al reported that among self-reported voice disorders female teachers revealed higher NHR and shimmer than normal group.[28] Thus, the acoustic parameters, NHR, and shimmer were suggested to be the major markers to reflect vocal abnormalities and to predict the subjective voice disorders. Therefore, highest F0, lowest F0, NHR, VTI, and ShdB are presumed to be the indicators of voice improvement among patients' age under 60 in this study. We also found that the VHI-10 scores of younger patients (age $<$ 60) were higher than older patients (age $\geq$ 60). Even if the sound quality was improved, it still cannot meet the requirements of daily life in younger patients with UVFP.

5. Conclusion

This research suggested Asian thyroid related UVFP patients who receive autologous fat surgery could statistically improve their lowest fundamental frequency (F0). Females showed lower Jita (Absolute Jitter) with statistical significance 1 year after operation. Highest F0, lowest F0, NHR, VTI, and ShdB (Absolute Shimmer, dB) maybe recommended to be the major post-operative evaluating markers of patients' age under 60. Voice parameters showed no significant correlation with BMI. This study rendered a detailed analysis of clinical prognostic parameters by different gender and age.

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