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Surgical effects of type-I thyroplasty and fat injection laryngoplasty on voice recovery

Akihito Hasukawa[a,b,*], Ryuichi Mochizuki[a,b,c], Hiramori Sakamoto[c], Akira Shibano[b], Tadashi Kitahara[a]

[a] Department of Otolaryngology and Head & Neck Surgery, Nara Medical University, 840 Shijo-cho, Kashihara-city, Nara 634-8522, Japan
[b] Department of Otolaryngology and Osaka Voice Center, Osaka Kaisei Hospital, Japan
[c] Sakamoto ENT clinic, Japan

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ABSTRACT

Objective: Type-I thryroplasty, also known as medialization thyroplasty (MT) and autologous fat injection laryngoplasty (FIL) are one of the main surgical treatments for unilateral vocal fold paralysis (UVFP). Both procedures have the same concept of completing the glottal closure by medializing the vocal fold, although the surgical approaches are quite different. In order to assess these surgical effects, we examined the treatment outcomes and benefits of the two surgeries.

Methods: We collected data from the 135 phonosurgeries that we performed out of 375 patients with UVFP at Osaka Voice Center, Osaka Kaisei Hospital from January 2009 to February 2013. After excluding cases with glottal level differences on phonation, either MT or FIL were performed on 80 cases. The inclusion criteria for the present study were: (1) patients had no history of previous phonosurgery, and (2) functional evaluations were available before/after surgery. Consequently, 43 participants (12 for MT and 31 for FIL) were enrolled in this study. Surgical effects were evaluated by means of the maximum phonation time (MPT), pitch period perturbation quotient (PPQ), amplitude perturbation quotient (APQ), and harmonic to noise ratio (HNR) just before, one month, and 6 months after surgery.

Results: Both MT and FIL showed significant improvement in MPT (MT, $p = 0.005$; FIL, $p < 0.001$) and PPQ (MT, $p = 0.047$; FIL, $p = 0.041$) at 1 month postoperation. We also compared the variation of each variable between the two procedures, but there were no significant differences in these parameters. However, MPT, APQ, and HNR at the post-MT after 6 months worsened compared to those at 1 month posttreatment, whereas MPT showed only a slight decrease from the 1st month to the 6th month in those with FIL.

Conclusion: Both MT and FIL were effective for the voice recovery in patients with UVFP. Our findings suggest that surgical results in FIL might be better than those in MT 6 months after surgery, although there were no significant differences between these two procedures 1 month postoperation.

* Corresponding author at: Department of Otolaryngology and Head & Neck Surgery, Nara Medical University, 840 Shijo-cho, Kashihara-city, Nara 634-8522, Japan.
E-mail address: hasukawa@naramed-u.ac.jp (A. Hasukawa).

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1. Introduction

Unilateral vocal fold paralysis (UVFP) causes varying degrees of dysphonia and increases the risk of aspiration due to glottic incompetency. The mainstays of surgical treatment for glottic insufficiency are either laryngeal framework surgery or injection laryngoplasty. Type-I thryroplasty also known as medialization thyroplasty (MT) is a representative of laryngeal framework surgery developed by Isshiki et al. [1]. It is considered as the gold standard for treatment of UVFP that involves medialization of the vocal fold with an implant inserted via the thyroid cartilage window. Injection laryngoplasty was introduced in 1911 by Brunings [2], which corrects the glottic incompetence by injection of filler material into the vocal fold or paraglottic space. Since autologous fat injection laryngoplasty (FIL) was first described in 1991 by Mikaelian et al. [3], autologous fat has become popular as injection material. Although the surgical approach is quite different, both procedures adhere to the same concepts to complete the glottal closure by medializing the vocal fold. And although each approach has advantages and drawbacks, no formal algorithm exists for the circumstances where either approach may be acceptable [4].

Several papers have reported treatment outcomes in MT [5–9] and injection laryngoplasty [10–14]; however, the direct comparison of the surgical results is rarely seen in these studies. To further compare the effects of these two procedures, we examined backgrounds and pre/posttreatment aerodynamic/acoustic parameters of patients with UVFP at our facility.

2. Materials and methods

This clinical study was approved by the Ethics Committee of Osaka Kaisei Hospital (identification number: 20-08).

2.1. Diagnosis

The surgical approach for UVFP, either with MT or FIL, was indicated after a watchful waiting period of about 6–12 months and/or voice therapy [15,16], or when recovery of motion was definitively not expected (surgical recurrent nerve sacrifice, or malignant invasion) [17]. After the waiting period, MT or FIL was considered to correct glottic incompetence by medializing the paretic vocal fold. The glottic incompetence, and also the passive movement of the arytenoid cartilage on the paralyzed side was detected by laryngoscopic observation [18]. The glottal level difference between the bilateral vocal folds caused by the location of the arytenoid cartilage during phonation was evaluated by CT scan. Accordingly, UVFP with height mismatch of the paralyzed and contralateral vocal folds required arytenoid adduction additionally to reduce the glottal level differences and incompetency [19,20].

2.2. Patients

We performed 135 phonosurgeries out of 375 patients with UVFP at Osaka Voice Center, Osaka Kaisei Hospital from January 2009 to February 2013. After excluding cases with glottal level differences on phonation, either MT or FIL were performed on 80 cases. To compare the effect of the two surgery, we did not evaluate the location of the paralyzed vocal fold to choose which surgery to perform by the degree of the glottal gap. Both procedures were presented to the patients, including the features of each treatment, advantages and/or disadvantages for the patients, as shown in Table 1 [4,17]. After they provided informed consent, these patients were allowed to choose freely, either procedure as their treatment strategy.

The inclusion criteria in the present study were as follows: (1) patients had no history of previous phonosurgery, (2) functional evaluations were available before/after surgery. Consequently, 43 participants (12 for MT and 31 for FIL) were enrolled in this study. Patients' backgrounds are shown in Table 2. There were significant differences in age, sex, and etiology, but the side of paralysis showed no statistical differences between MT and FIL.

2.3. Surgery

MT was performed in the operating room with local anesthesia. As described by Isshiki et al., an implant was inserted through an externally created window in the thyroid lamina at the level of the vocal fold, to medialize and augment the affected vocal fold. The position and volume of the implant were adjusted under transnasal laryngoscopic observation of the vocal folds so as to move the affected vocal fold into the median position and to improve the voice quality [1]. As an implant, hydroxyapatite was used for 10 patients, and expanded polytetrafluoroethylene (ePTFE, Gore-Tex®) was used for 2 patients. The insertion techinique did not differ by the type of an implant.

FIL was performed in the operating room transorally under general anesthesia by using microscopic suspension laryn-

Table 1. Features of type-I thyroplasty and autologous fat injection laryngoplasty.

	Anestesia	Direct voicing and vocal fold vibration feedback during the procedure	External Incision	Risk of reabsorption of the implant
MT	Local	Able	Necessary	No (hydroxyapatite, ePTFE)
FIL	General	Unable	Unnecessary	Yes (autologous fat)

Both procedures were presented to the patients, including the features of each treatment that could be advantageous and/or disadvantageous for the patients. This table is based on the references 4 and 17.
MT = type-I thyroplasty, FIL = autologous fat injection laryngoplasty, ePTFE = expanded polytetrafluoroethylene.

Table 2. Patients' backgrounds.

		MT		FIL		
		No. or yr	Percent	No. or yr	Percent	*p* value
Age at intervention(mean±SD)		65.6 ± 10.7		50.6 ± 14.1		0.002
	Range	48-86		17-72		
Gender						0.037
	Male	8	67	9	29	
	Female	4	33	22	71	
Side of paralysis						0.698
	Left	10	83	22	71	
	Right	2	17	9	29	
Etiology						0.003
	Postsurgery *					
	Thyroid surgery	1	8	10	32	
	Lung cancer surgery	4	33	0	0	
	Aorta replacement	0	0	3	10	
	Esophageal cancer surgery	1	8	0	0	
	Vagal schwannoma surgery	0	0	1	3	
	Spine surgery	0	0	1	3	
	Mediastinal lymphagioma surgery	0	0	1	3	
	Neoplasm **					
	Thyroid cancer	1	8	3	10	
	Lung cancer	2	17	0	0	
	Thoracic tumor of unknown primary cancer	1	8	0	0	
	Mediastinal lymph node metastasis from breast cancer	0	0	1	3	
	Aortic arch aneurysm	1	8	0	0	
	Scleroderma	0	0	1	3	
	Tracheal intubation	0	0	1	3	
	Pulmonary tuberculoma	0	0	1	3	
	Laryngeal Herpes Zoster	0	0	1	3	
	Idiopathic	1	8	7	23	
Total		12		31		

There were significant differences in age, sex, and etiology, but the side of paralysis shows no statistical differences between type-I thyroplasty and autologous fat injection laryngoplasty. Fisher's exact test was used for the dichotomous variables, and unpaired t-test was used for continuous variables. SD = standard deviation, MT = type-I thyroplasty, FIL = autologous fat injection laryngoplasty, * = Developed hoarseness after the surgery, ** = Developed hoarseness before the treatment.

goscopy. For all the cases, autologous fat was used as an injection material, harvested by lipo-suction technique from the lower abdomen, just below the umbilicus. It was injected into the middle and lateral part of the membranous portion of the vocal fold within the thyroarytenoid muscle layer and also at the area posterior lateral to the vocal process. This technique has been previously described by Sato et al. [21].

2.4. Follow-up

Patients both in MT and FIL groups were evaluated just before, approximately one month after, and 6 months after surgery, for the following voice parameters.

The maximum phonation time (MPT), as a simple indicator of glottis closure, was documented for each patient. MPT consisted of the longest period of time while phonating a vowel sound (/a/) at a comfortable pitch and loudness level in three efforts.

Acoustic voice analysis was performed, using Multi-Dimensional Voice Program (MDVP, KayPentax, Lincoln Park, NJ, USA) for all the 43 patients. All testing was performed in a quiet room with a mouth-to-microphone distance of 10 cm. Analysis was performed from a sustained vowel sound (/a/) at a comfortable pitch and intensity level. Values of the following parameters were analyzed: pitch period perturbation quotient (PPQ), amplitude perturbation quotient (APQ), and harmonic to noise ratio (HNR) converted from noise to harmonic ratio (NHR) by the following calculation formula:

$$HNR = 10 \times \log_{10}(1/NHR) \quad (1)$$

PPQ and APQ developed by Koike et al. [22,23] are the parameters of period-to-period variability (perturbation) of the pitch period or amplitude, with a smoothing factor to exclude the effect of long-term trend of the pitch period or amplitude. In MDVP, PPQ is evaluated with smoothing factor of 5 periods and APQ is evaluated with smoothing factor of 11 periods [24]. HNR developed by Yumoto et al. [25], is an acoustic energy ratio of the harmonic component to the noise component.

These 3 parameters are designed to reflect the acoustic aspects of voice quality.

2.5. Statistics

Wilcoxon signed-rank test was used to compare pretreatment and posttreatment voice changes for both treatment groups. Mann-Whitney U test was used to compare the pretreatment parameters of each variable between the MT and FIL groups. Repeated two-way analysis of variance (ANOVA)

Table 3. Pretreatment functional parameters.

	MT mean±SD	FIL mean±SD	*p* value
	(n = 12)	(n = 31)	
MPT(s)	5.4 ± 5.5	7.6 ± 6.8	0.168
	(n = 10)	(n = 27)	
PPQ(%)	3.35 ± 3.04	2.77 ± 3.12	0.699
APQ(%)	7.27 ± 5.41	7.87 ± 6.99	0.775
HNR(dB)	6.41 ± 3.34	6.79 ± 2.62	0.986

Pretreatment functional parameters were obtained just before surgery. There were no significant differences in any parameters between type-I thyroplasty and autologous fat injection laryngoplasty. Mann–Whitney U test was used to compare the two groups.
MPT = maximum phonation time, PPQ = pitch perturbation quotient, APQ = amplitude perturbation quotient, HNR = harmonic to noise ratio, SD = standard deviation, MT = type-I thyroplasty, FIL = autologous fat injection laryngoplasty.

was used to compare the improvement between the two groups. To compare the patients' backgrounds, Fisher's exact test was used for the dichotomous variables, and unpaired t-test was used for continuous variables. IBM SPSS version 25 (IBM, Armonk, NY, USA) was used for the statistical calculations in this study. Significance level was accepted at $p < .05$ in two-tailed tests.

3. Results

Pretreatment functional parameters obtained just before surgery are shown in Table 3. In the pretreatment acoustic analysis, the parameters that were not obtained from 2 patients from MT group and 4 patients from FIL group due to the severe hoarseness. There were no significant differences in any parameters between MT and FIL groups.

Posttreatment functions were evaluated approximately one month (range 13-45 days) and 6 months (range 112-202 days) after surgery.

3.1. Postoperative outcomes of MT at one month

As shown in Fig. 1A, MT yielded significant improvement (increase) in MPT (s) (pretreatment 5.4 ± 5.5, posttreatment 10.7 ± 5.0, $p = 0.005$) in 12 patients with UVFP one month after surgery. In 10 patients, who were able to obtain pretreatment acoustic parameters, PPQ (%) (pretreatment 3.35 ± 3.04, posttreatment 1.63 ± 1.55, $p = 0.047$) showed significant improvement (decrease) after treatment. Although statistical significance was not detected in APQ (%) (pretreatment 7.27 ± 5.41, posttreatment 5.76 ± 4.49, $p = 0.333$) or in HNR (dB) (pretreatment 6.41 ± 3.34, posttreatment 7.51 ± 2.43, $p = 0.260$), a trend toward improvement (decrease in APQ, increase in HNR) was clearly demonstrated.

3.2. Postoperative outcomes of FIL at one month

As shown in Fig. 1B, FIL yielded significant improvement (increase) in MPT (s) (pretreatment 7.6 ± 6.8, posttreatment 13.5 ± 7.0, $p < 0.001$) in 31 patients with UVFP one month after surgery. In 27 patients, who were able to obtain pretreatment acoustic parameters, PPQ (%) (pretreatment 2.77 ± 3.12, posttreatment 1.30 ± 1.02, $p = 0.041$) showed significant improvement (decrease) after treatment. Although statistical significance was not detected in APQ (%) (pretreatment 7.87 ± 6.99, posttreatment 4.72 ± 2.77, $p = 0.113$) or in HNR (dB) (pretreatment 6.79 ± 2.62, posttreatment 7.64 ± 1.51, $p = 0.532$), these parameters showed improvement (decrease in APQ, increase in HNR) after treatment.

3.3. Postoperative outcomes of MT vs. FIL at one month

We also compared the pretreatment and one month posttreatment parameters of the two procedures by repeated two-way ANOVA, but there were no statistically significant interactions or differences between the two groups in MPT (interaction $p = 0.822$, difference between groups $p = 0.110$, difference between time $p = 0.001$), PPQ (interaction $p = 0.842$, difference between groups $p = 0.468$, difference between time $p = 0.012$), APQ (interaction $p = 0.556$, difference between groups $p = 0.869$, difference between time $p = 0.097$) or HNR (interaction $p = 0.849$, difference between groups $p = 0.690$, difference between time $p = 0.126$).

3.4. Postoperative outcomes of MT vs. FIL at six months

As shown in Table 4, MPT at the posttreatment 6th month were able to obtain in 6 and 10 patients from MT and FIL groups, respectively. Of those patients, acoustic parameters such as PPQ, APQ, and HNR were managed to obtain in 6 and 7 cases in MT and FIL groups, respectively. Although the sample size at the posttreatment 6th month were too small and limited to conduct a meaningful statistical analysis, the data profiles of the 1st and 6th months showed trend of voice recovery. In the MT group, mean MPT, APQ, and HNR at the posttreatment 6th month worsened compared to that at the 1st month posttreatment, whereas only MPT showed a slight decrease from the 1st month to the 6th month in the FIL group.

4. Discussion

The purpose of this study was to compare the two types of phonosurgery in a short period of one month after the operation of patients with UVFP. MT and FIL were both effective for UVFP, and there were no significant differences between the two procedures at least one month after the surgery, consistent with results described in previous reports [26,27]. According to previous studies, surgical effects of MT on vocal recovery at the postoperative 1st month could last more than 1 year [28,29]. On the other hand, effects of FIL 1 month after surgery lasted for 6-12 months [11,12]. Therefore, we might expect long-term favorable outcomes of both procedures at our facility.

Among the voice assessment parameters used in this study, MPT and PPQ showed significant improvement, but APQ and HNR did not. MPT is the most frequently used parameter in

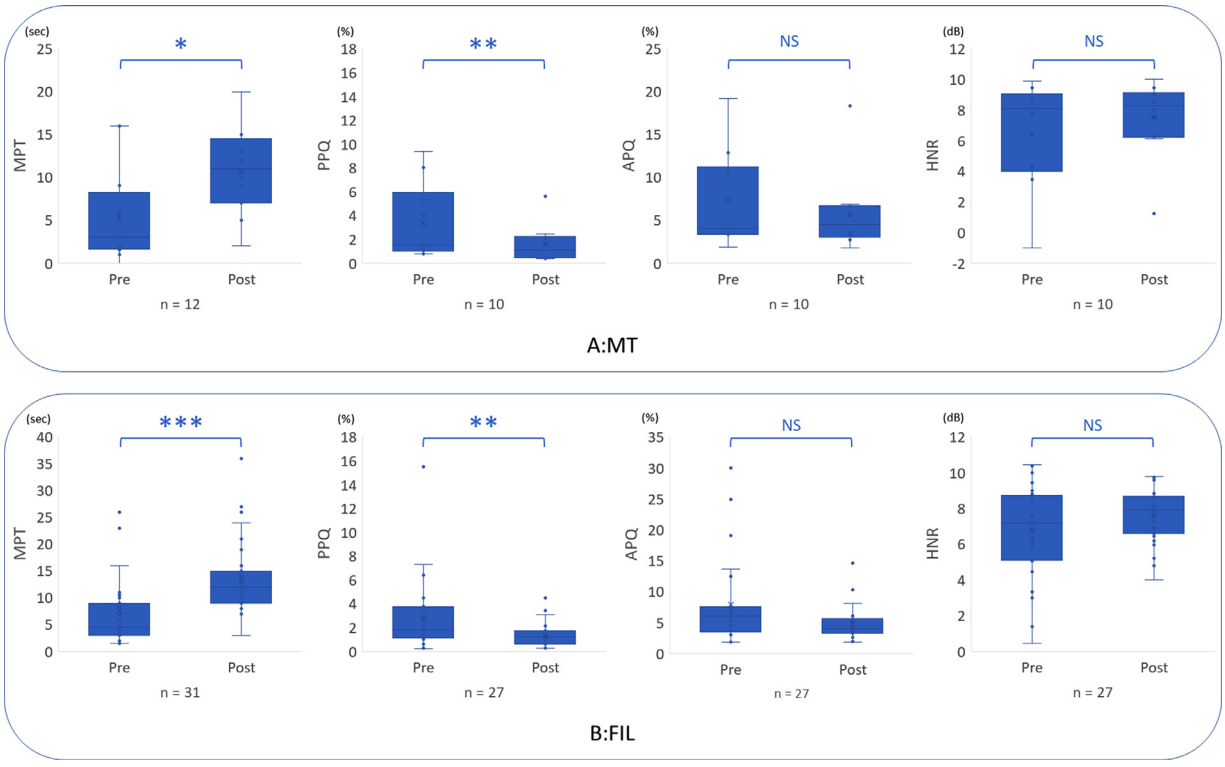

Fig. 1. Changes in aerodynamic and acoustic parameters one month after type-I thyroplasty (A: MT) and autologous fat injection laryngoplasty (B: FIL). Type-I thyroplasty and autologous fat injection laryngoplasty showing significant improvement in MPT and PPQ in patients with unilateral vocal fold paralysis one month after surgery. Although statistical significance was not detected in APQ or HNR, a trend toward improvement is clearly demonstrated. Wilcoxon signed-rank test was used to compare pretreatment and posttreatment voice change for both treatment groups. MPT = maximum phonation time, PPQ = pitch perturbation quotient, APQ = amplitude perturbation quotient, HNR = harmonic to noise ratio. * = $p < 0.01$, ** = $p < 0.05$, *** = $p < 0.001$, NS = not significant.

Table 4. Changes in aerodynamic and acoustic parameters six months after type-I thyroplasty and autologous fat injection laryngoplasty.

		MT				FIL		
		Pre	Post 1m	Post 6m		Pre	Post 1m	Post 6m
MPT(s)	n = 6	8.6 (1.5-16.0)	13.8 (10.0-20.0)	10.6 (4.5-15.0)	n = 10	4.7 (1.5-9.0)	10.7 (7.0-15.0)	9.9 (4.0-25.0)
PPQ(%)	n = 6	4.69 (1.81-12.87)	3.36 (1.75-5.48)	3.32 (2.19-4.71)	n = 7	2.51 (0.61-6.37)	1.95 (0.34-4.50)	1.36 (0.22-3.30)
APQ(%)		1.76 (0.77-5.26)	0.66 (0.40-1.69)	0.92 (0.36-1.86)		8.69 (3.72-24.93)	5.59 (1.85-10.31)	3.74 (1.49-7.59)
HNR(dB)		8.14 (4.15-9.87)	8.69 (6.11-10.00)	8.60 (8.15-10.00)		6.16 (1.39-8.73)	6.99 (4.00-8.63)	8.56 (6.27-9.79)

Although the sample size at the 6th month posttreatment was too small and limited to conduct an accurate statistical analysis, the data profiles at the 1st and 6th month showed trends of voice recovery. In the type-I thyroplasty group, mean MPT, APQ, and HNR at the 6th month posttreatment worsened compared to that at the 1st month posttreatment, whereas only MPT showed a slight decrease from the 1st month to the 6th month in the autologous fat injection laryngoplasty group.
MPT = maximum phonation time, PPQ = pitch perturbation quotient, APQ = amplitude perturbation quotient, HNR = harmonic to noise ratio, MT = type-I thyroplasty, FIL = autologous fat injection laryngoplasty, Pre = pretreatment, Post 1m = posttreatment 1st month, Post 6m = posttreatment 6th month.
Results represent mean (range).

voice evaluation, and it is a significant voice outcome indicator in terms of pre- and post-operative change [30]. In fact, the improvement of MPT was more significant than that of PPQ in present study. As an aerodynamic evaluation, mean flow rate (MFR) is also useful. But we were able to evaluate MFR only from few patients participated in this study, and lung capacity data were not available. From the parameters of acoustic analysis, we used PPQ, APQ, and HNR. Additionally, Jitter and Shimmer are the other commonly used acoustic analysis parameters [30] that quantify short-term variation in period and amplitude [31]. Short-term variations (perturbations), which is assumed to reflect voice disorders, are affected by long-term fluctuations (trend lines) that exist in human vowel phonation. The PPQ and APQ were used in the present study, because they include a measurement parameter that attenuates the influence of trend lines from perturbations expressed by Jitter and Shimmer respectively [32]. These parameters are supposed to be strongly correlated with each

other [33]. However, Jitter is affected mainly by poor control of vocal fold vibrations and higher percentage of jitter is likely to appear frequently in pathological voices. As for Shimmer, it might increase with the reduction of glottal resistance and when there is a mass lesion on the vocal folds, and it is associated with the presence of noise emission and breathiness [34]. Moreover, HNR is supposed to be affected by both amplitude and frequency perturbations [35]. These differences in the characteristics of each acoustic analysis parameter and the difference in smoothing factors that reduce the influence of trend lines in PPQ and APQ [24,36] might have caused the different results between the acoustic analysis parameters.

UVFP cases with infeasible preoperative acoustic analysis were excluded from statistical analysis in the present study. However, even in those excluded cases, acoustic analysis became feasible after both MT and FIL, and MPT were found to be improved (data not shown). The parameters were not obtained by acoustic analysis because the fundamental frequency (F0) could not be detected and measured in cases with severe hoarseness. Therefore, in such cases, by both surgical procedures, the voice recovered to the point that postoperative analysis was possible. The value of existing acoustic analysis as an index of therapeutic effect has been questioned [37]. There are limitations of the evaluation method itself, such as inaccurate and impossible frequency detection depending on the type of voice, as seen in the case that could not undergo preoperative analysis in this study [31]. The development and popularization of useful and practical theories and devices are eagerly awaited, which include the acoustic analysis methods based on new frequency detection [38] or independent of frequency detection [39–41].

As shown in Table 4, a small number of patients could be followed 6 months after surgery. As a result, in MT that has the advantage of no implant absorption, the speech improvement performance deteriorated over a long-term postoperative period. MT involves a risk of post-operative soft-tissue reaction and edema, shifting or extrusion of the implant, and hemorrhage [42]. Iwahashi et al. reported factors that cause poor outcome of MT, such as a small implant size, undercorrection of the vocal fold, antero-posterior implant malposition, and the use of ePTFE [43]. In the present study, the worsening of results at the 6th month may have been caused by the following: an under correction of the vocal folds revealed by edema alleviation over the long-term postoperative period and a shifting of appropriately placed implant to the anterior-posterior direction by the time course. Furthermore, since MT approaches from the outer side of the membranous part of the vocal fold, it is difficult to correct the disuse atrophy of the paralyzed vocal fold in the affected side as compared to FIL. Moreover, the MT group is significantly older than the FIL group, resulting in the age-related vocal fold atrophy in the contralateral side, which causes the subsequent deterioration in voice. On the other hand, FIL is a relatively minimally invasive surgical method [13], although there have been reports of cases where reoperation was performed due to postoperative fat prolapse from the injection site, and postoperative fat absorption [20]. When compared with MT, it is suggested that edematous changes around the vocal folds that may have occurred in the early postoperative period were so mild as to have smaller effect on the results 1 to 6 months after surgery.

In the present paper, two types of implant were used to perform MT. As mentioned previously, Iwahashi et al. reported use of ePTFE is one of the factors that causes poor outcome of MT [43]. Although the difference by the implant choice were not able to prove statistically since the number was too small (2 ePTFE cases vs 10 hydroxyapatite cases), the mean MPT of pre/postoperation was similar (pre 6.0s vs 5.3s, post 10.3s vs 12.5s). This data shows that the type of implant did not effect the result of MT in this report.

There were two major limitations in the present study. First, the size of study samples was relatively small and the period of patients' follow-ups was relatively short. Since our facility is situated in the center of Osaka City, patients were usually busy and rarely do these patients return after long period of time if they are doing well, even when they were are encouraged to return for follow-up examinations. Studies with larger samples and follow-up periods will be reported subsequently. Second, the study design was not a randomized controlled but a retrospective case control. Therefore, there were significant differences in patients' demographic characteristics such as age, sex, and etiology, as seen in Table 2. And it also resulted in differences in number of patients between groups. By these limitations, the result may change by adding several cases. Moreover, the surgical selection might involve a risk of bias with regard to both the surgeons as well as the patients. For example, the surgeons had a tendency to recommend MT with local anesthesia to patients who had contraindications to general anesthesia, such as a post lung cancer group. On the other hand, the patients who had experienced external incision earlier tended to insist on FIL to avoid another neck incision, such as a post thyroid surgery group. Despite the limitations, no significant differences were noted in pretreatment parameters between 12 cases of MT and 31 cases of FIL, as presented in Table 3, thereby indicating that comparing treatment results of these two procedures were reliable.

Regarding patients' backgrounds and surgical selection based on Table 2, MT was performed on patients with UVFP due to lung cancer or its surgery and FIL was mainly performed on those with thyroid cancer or thyroid disease-related surgery. Treatment outcomes were favorable with both procedures, indicating that the surgical selection was appropriate in each case based on patients' backgrounds. Although there has not yet been any international consensus on surgical treatments for UVFP with no glottal level difference on phonation, the present findings suggest good examples for decision-making on surgical selection.

5. Conclusion

Both of MT and FIL were effective to the voice recovery in patients with UVFP. It is suggested that surgical results in FIL might be better than those in MT 6 months after surgery,

although there were no significant differences between these two procedures at the postoperative 1st month.

Declaration of Competing Interest

The present study does not include any conflicts of interest.

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