The Montgomery Thyroplasty Implant System: A 360° Assessment

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CHAPTER 4:

Very long term voice handicap index voice outcomes after Montgomery thyroplasty: a cross-sectional study.

Abstract:

Objective

The aim of this multi-centric cross-sectional study was to examine the permanency of Montgomery Thyroplasty (MTIS) results from a patient's perspective.

Design

The study consisted of collecting Voice Handicap Index (VHI-30) questionnaires from patients who had been previously been operated with MTIS between 2 and 12 years before. Very long term (>2 years) post-operative data were compared to the previously acquired pre-operative and early post-operative VHI results. Influence of factors such as age, gender, size/side of the prosthesis, and length follow-up were also analyzed.

Setting

Multi-centric study involving three tertiary European voice centers.

Participants

Forty-nine Unilateral Vocal Fold Paralysis (UVFP) patients, treated by MTIS, were included in the study .

Main Outcome Measures

The Voice Handicap Index-30 score.

Results & Conclusions

The median VHI was significantly different over time-points (Friedman's test $p<0.001$), with a significant difference between pre-operative and early post-operative time point (median VHI: 70 vs 21, respectively; $p<0.001$) and between pre-operative and very-long-term post-operative time-point (median VHI: 70 vs 16, respectively; $p<0.001$). The median VHI did not differ for the early and very-long -term post-op time-point (median VHI: 21 vs 16; $p=0.470$).

Age differences, gender differences and size/side differences of the prosthesis, centers where surgery took place and length of the follow-up showed no significant influence.

MT (medialization thyroplasty) overall and MTIS in particular, should be considered as a possible standard of care for UVFP when permanency of voice results is sought.

Introduction

Unilateral Vocal Fold Paralysis (UVFP) in abduction is responsible for breathy voice, phonatory dyspnea and, in some cases, dysphagia. Many treatments have been advocated in the past for this debilitating condition. Besides voice therapy, four different surgical procedures have been proposed as treatment for UVFP: the medialization thyroplasty (MT), the injection laryngoplasty (IL), the arytenoid adduction or pexy (AA) and the laryngeal reinnervation (LR). These techniques can be combined. All four of these interventions have shown satisfactory short and long term post-operative results.

Unfortunately, the difference between short -or early- and long term post-operative results regarding UVFP surgery is not clearly defined. A recent literature review revealed that the term "short-term" is used up to 14 months after surgery while the term "long-term" is already used 12 months after surgery, creating some semantic confusion [1]. For more clarity, we defined very long term results, as results that were obtained, at least, 2 years after surgery.

All the surgical techniques mentioned above have their advantages and limitations. Among them MT presents a relatively low technical challenge. This is even more true for MT using the Montgomery Thyroplasty Implant System (MTIS) for which a short learning curve has been shown [2]. MT is also reputed to be a one-time procedure assuring long terms results. So much so that many authors consider MT as the gold standard for permanent treatment of UVFP. Concerns remain, however, about the permanency of the results of MT due to possible vocal fold atrophy over time [3, 4].

Only four studies address the very long term results of MT as defined by this study. None of these studies investigate MT performed with the MTIS. One of these studies is a case series of 5 patients [5], two look at voice results in terms of acoustics and aerodynamics parameters [6,7], the last study looks at the voice results in terms of Voice-Related Quality of Life parameter [8]. This last study concluded that "Patients that were more distant from surgery had lower V-QROL scores than those who had more recently been treated". In other words, the only very long term study investigating voice results from a patient's perspective demonstrates a fading of voice results in terms of voice-related quality of life in the course of time.

In order to assess very long term voice results for patients undergoing a MT with the MTIS, we launched a multi-centric cross sectional study collecting Voice Handicap Index questionnaires (VHI-30) from patients operated at least two years before. These very long term post-operative data were compared to the previously acquired pre-operative and the short term post-operative VHI results.

Influence of factors such as age, gender, size/side of the prosthesis, and length follow-up were also analyzed.

Material and Method

The study protocol has been approved by the Ethical Committees of all participating institutions.

Patients, from 3 different treatment centers practicing the MTIS and meeting the inclusion criteria, were included.

To be included in the protocol, patients had to have undergone a MTIS -with no associated procedure- for a UVFP, at least 2 years before inclusion. The UVFP had to be of neurogenic origin as defined by the ELS guidelines [9]. There was no length of time limit for the follow-up. Patients had to be aged between 18 years and 80 years at the time of the MTIS. All patient's files had to include a pre-op VHI-30 questionnaire and an early post-op VHI-30 that had been performed less than 12 months before and less than 14 months after the MTIS respectively. Fourteen months was chosen as this was found to be the cut-off between short and long term post-op according to the literature. In case of multiple post-operative early VHI-30 assessments, the earliest data were considered for the study. The VHI-30 must have been validated and published for the language of use.

A careful electronic medical record (EMR) review excluded deceased patients and patients that had to undergo further voice surgeries after the MTIS.

This study is a cross-sectional, survey based, multi-centric study filed on NIH's ClinicalTrials.gov under the number NCT02969993 (first received November 18th 2016).

The study consisted of collecting Voice Handicap Index (VHI-30) questionnaires from patients who had been previously been operated with MTIS at least 2 years before.

The questionnaires were obtained in two different ways. In case of center 1 and 3, VHI-30 questionnaires were sent out by mail accompanied by an introduction letter and an informed consent that had to be returned. The patient certified having filled in the VHI-30 personally, with no assistance whatsoever. Furthermore, patients were asked to disclose possible further voice surgeries or new disease or condition that could affect their voice quality. It was also possible for relatives to communicate about the death of the patient by returning the mail.

In case of center 2, patients were invited by phone, to come to the hospital to fill in the VHI-30 along with an informed consent. Questions about possible further voice related surgeries or conditions that could affect their voice quality were checked by phone. Patients were isolated alone in a room in order to personally fill in the VHI-30 questionnaire.

Dead patients reported by relatives and patients presenting post MTIS surgeries or diseases/ conditions that would affect voice quality were excluded and not considered for the study.

All 3 centers entered their data in one Excel data bank and included: anonymized identification of the patient, date of birth, gender, side and size of the prosthesis, date of the MTIS procedure, date and value of pre-operative VHI-30, date and value of early post-operative VHI-30 and date and value of very long term post-operative VHI-30. Inclusion and exclusion data were also checked for each center.

Once data was obtained, very long term (>2 years) post-operative data were compared to the previously acquired pre-operative and early post-operative VHI results. Influence of factors: age, gender, size/side of the prosthesis, center where surgery has been performed and length of VHI-30 follow-up were also analyzed.

Continuous variables were summarized using medians, interquartile ranges and ranges. To analyze the evolution of VHI in time (repeated measurements: pre-operative, early and very-long-term post-operative), Friedman's rank sum test, a non-parametric alternative to the parametric test one-way repeated measures ANOVA, was used. A pairwise comparison using Nemenyi multiple comparison test was then applied to identify significant differences between time period groups. Variables associated with the decrease in VHI over time were assessed using random effects-expectation maximization (RE-EM) tree, a mixed effects model for longitudinal data, to take into account repeated measurements. Time period and patient identifier were inserted as random effects to take into account repeated measures for each patient. The center was assessed as a fixed effect in the model because of the low number of categories (3 centers).

Results

Eighty-two (82) patients were considered for the study, as they had undergone a thyroplasty using MTIS for UVFP, as a sole procedure, that had been performed at least two years earlier. The number of deceased patients according to the data available in their EMR were 13, 1 and 0 for center 1, 2 and 3 respectively. In none of the cases the cause of death was related to the MTIS. The EMR review revealed one patient that underwent a complimentary injection laryngoplasty (IL) after MTIS because of unsatisfactory voice result. This additional procedure was performed within 2 years postoperatively. Therefore, in total 15 of the initial 82 patients were excluded from the study.

The 67 remaining patients were asked to participate in the study. The VHI-30 score along with an accompanying letter and an informed consent form, to be returned, were sent to 33 patients from center 1 and 16 patients from center 3. Eighteen patients from center 2 were invited by phone to fill in the VHI-30 questionnaire at the hospital.

The overall response rate was 78% (81% for center 1, 89% for center 2 and 56% for center 3).

Relatives informed authors of the death of 2 patients from center 1. Moreover, one patient from center 1 informed authors about the occurrence of a voice impairing disease (the recurrence of metastatic thyroid papillary carcinoma for which he was treated with external radiotherapy). These patients were categorized as non-responders and excluded from the study. Finally 49 patients were included in the study (24 from center 1, 16 from center 2 and 9 from center 3).

Table 1 shows the patients characteristics of the cohort.

	Median [P25; P75] (min-max) or n (%)
Age at time of surgery, years	52.9 [42.3; 61.8] (16.3 – 74.5)
Females	34 (69.4)
Prosthesis	
Side : left	32 (65.3)
Size	9 [8; 10] (6 – 12)
Size : large*	34 (69.4)
Center	
Center 1	24 (49.0)
Center 2	16 (32.6)
Center 3	9 (18.4)
Time between date pre-op VHI and date surgery, in months	3 [1; 3] (0 – 12)
Time between date early post-op VHI and date surgery, in months	1 [1; 2] (0 – 14)
Time between date very long term post-op VHI and date surgery, in months	55 [42; 66] (24 - 142)

* ≥10 for males and ≥9 for females

Table 1: Patients characteristics at the time of MTIS (n=49)

The median time between the pre-operative VHI-30 and the procedure was 3 months. The median latency for early post-operative VHI-30 was 1 month (0-14 months) and the median latency for very-long-term post-operative VHI-30 was 55 months or 4,5 years (2-11,8 years).

The median [P_{25}; P_{75}] VHI score was 70 (59; 84] before the MTIS. It decreased to 21 [9; 37] and 16 [9; 30] in the early and very long term post-operative period respectively. The median VHI was significantly different over the 3 time points (Friedman's test $p<0.001$) with a significant difference between pre-op and early post-op (median VHI: 70 vs 21, respectively; $p<0.001$) and between pre-op and very-long-term post-op time points (median VHI: 70 vs 16, respectively; $p<0.001$). The median VHI did not differ significantly between early and very-long-term post-op time points (median VHI: 21 vs 16; $p=0.470$).

Figure 1 displays the linear graph (a) and boxplots (b) showing the evolution of VHI-30 scores over time in all patients.

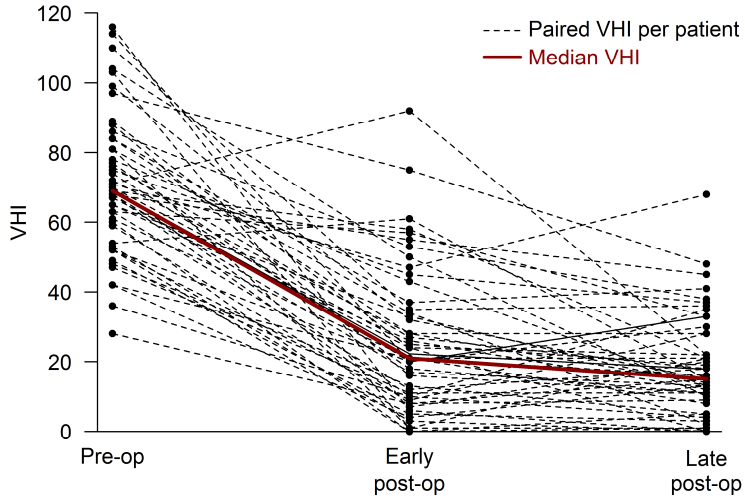
The cohort was grouped by their latency period, i.e. the period between the MTIS and the moment the very long term post-operative VHI-30 was scored. Two types of grouping were performed. The first grouping compared three latencies in years (from 2 to 4 years, from 4 to 8, longer than 8 years). The second grouping compared three latencies in months offering three comparable groups in terms of number of months (<40 months, 40 - 59 months and ≥ 60 months of latency).

Tables 2 shows the difference in VHI-30 between different time-points for the three different groups of latencies calculated with both grouping techniques. Results indicate no statistical difference of VHI-30 between early and very long term post-operative assessment up to 8 years and more of follow-up. This indicates a strong stability of voice results over time.

Four variables possibly influencing these results were analysed through the RE-EM tree technique. Results for age differences, gender differences and size/side differences of the prosthesis are displayed in Figure 2. None of these variables showed a significant effect on previously mentioned results.

A possible "centre" effect was also statistically ruled-out. Figure 3 displays a boxplots comparing VHI-30 results by centers.

A



B

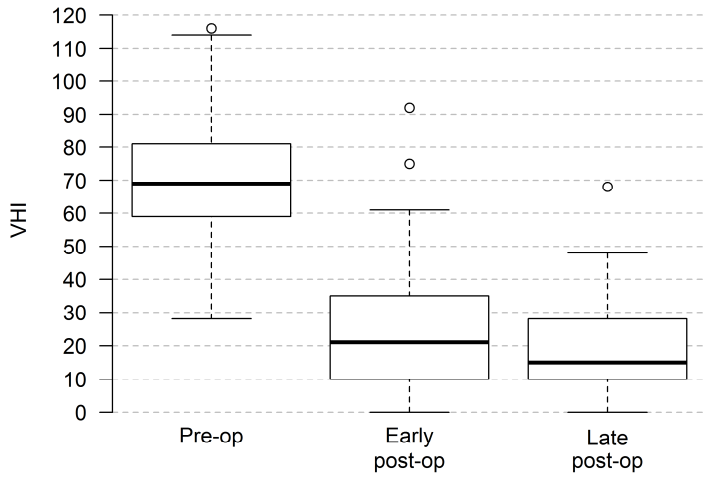


Figure 1: Linear graph (a) and boxplot (B) showing the evolution of VHI-30 scores over time in all patients

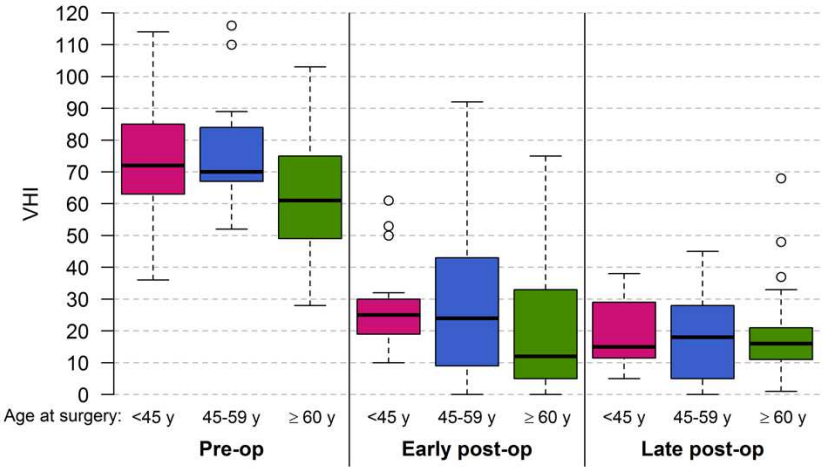
A

	<48 months (4yrs) (n=19)	Latency time 48-95 months (4-8yrs) (n=22)	≥96 months (8yrs) (n=8)	p-value
VHI, median [P_{25}; P_{75}] (min; max)				
Pre-op	69.0 [56.5; 82.0] (42.0; 110.0)	66.0 [52.3; 81.0] (28.0; 116.0)	72.0 [68.0; 78.0] (61.0; 84.0)	0.724
Early post-op	24.0 [9.0; 50.0] (0.0; 92.0)	17.0 [8.3; 27.5] (1.0; 57.0)	26.0 [20.8; 30.3] (17.0; 55.0)	0.232
Late post-op	20.0 [11.0; 27.5] (1.0; 68.0)	12.5 [4.8; 20.3] (0.0; 37.0)	23.5 [16.8; 32.8] (8.0; 45.0)	0.101
Difference pre-op and early post-op	-35.0 [-60.0; -23.0] (-102.0; 21.0)	-44.0 [-57.8; -38.3] (-110.0; -6.0)	-48.0 [-51.8; -43.8] (-56.0; -13.0)	0.565
Difference pre-op and very long term post-op	-49.0 [-62.0; -41.0] (-82.0; -3.0)	-53.0 [-78.5; -36.5] (-116.0; -1.0)	-52.0 [-55.3; -43.8] (-58.0; -23.0)	0.791
Difference early and very long term post-op	-5.0 [-23.5; 3.0] (-70.0; 21.0)	-4.0 [-14.0; 4.5] (-40.0; 25.0)	-5.0 [-9.3; 1.0] (-13.0; 10.0)	0.959

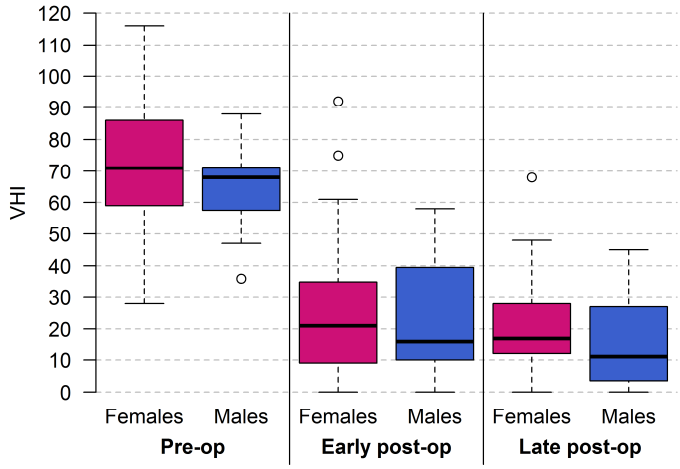
B

	<40 months (n=15)	Latency time 40-59 months (n=21)	≥60 months (n=17)	p-value
VHI, median [P_{25}; P_{75}] (min; max)				
Pre-op	68.5 [53.5; 74.8] (42.0; 103.0)	71.0 [58.0; 82.3] (28.0; 116.0)	68.0 [61.0; 81.0] (49.0; 114.0)	0.850
Early post-op	22.5 [11.8; 54.3] (1.0; 92.0)	14.0 [7.5; 33.5] (0.0; 75.0)	25.0 [20.0; 32.0] (3.0; 57.0)	0.329
Late post-op	21.0 [15.8; 24.8] (5.0; 68.0)	12.0 [0.0; 15.8] (4.8; 48.0)	19.0 [12.0; 30.0] (0.0; 45.0)	0.089
Difference pre-op and early post-op	-32.5 [-54.0; -18.5] (-102.0; 21.0)	-47.5 [-60.0; -34.3] (-110.0; -20.0)	-47.0 [-51.0; -40.0] (-94.0; -6.0)	0.246
Difference pre-op and very long term post-op	-45.5 [-51.5; -35.8] (-82.0; -3.0)	-56.5 [-68.8; -43.3] (-116.0; -1.0)	-53.0 [-56.0; -43.0] (-84.0; -23.0)	0.279
Difference early and very long term post-op	-3.5 [-20.5; 13.0] (-70.0; 21.0)	-5.5 [-15.5; 2.0] (-40.0; 25.0)	-4.0 [-13.0; 0.0] (-32.0; 19.0)	0.981

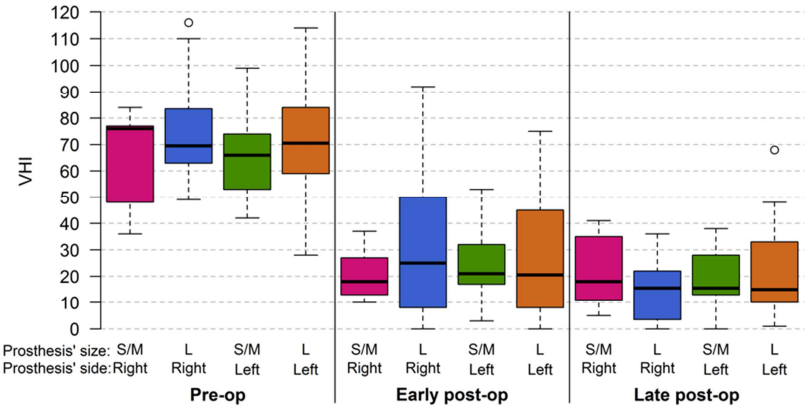
Table 2: VHI decrease according to the time since the surgery (N=49). Latency times in years (A). latency times in months (B)



A: results by age of the patient at the age of MTIS



B: results by gender



C: results by size of prosthesis

Figure 2: Boxplots comparing pre-operative, early post-operative and late post-operative VH1-30 results for various variable grouping of the cohort. (A) age of patients at the time of MTIS, (B) gender of patients, (C) small and medium (S/M), or large (L)Montgomery prosthesis used. A large prosthesis is defined as being ≥ size 9 for female patients and ≥ size 10 for male patients.

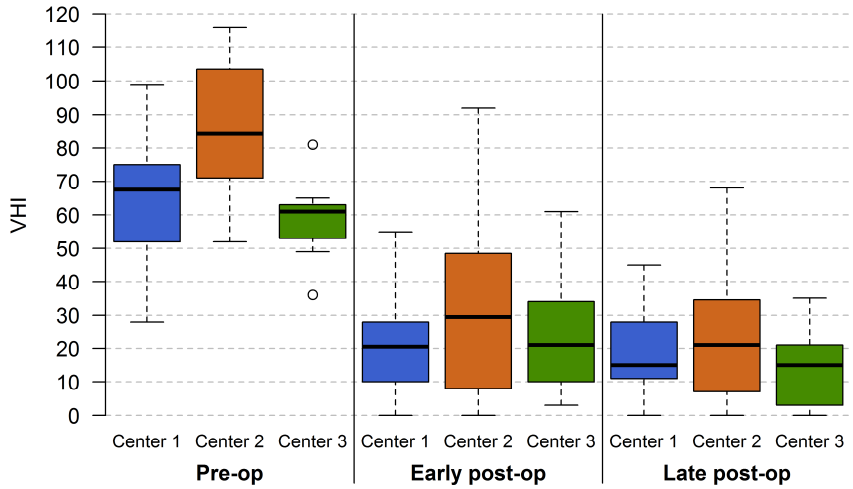


Figure 3: Boxplots comparing pre-operative, early post-operative and late post-operative VH1-30 results by center.

Discussion

Unilateral Vocal Fold Paralysis (UVFP) has been defined in a consensus paper by Rosen et al. as unilateral vocal fold immobility of neurogenic origin [9]. MT is considered by a majority of authors as a "permanent" treatment of UVFP. There is a lack of data that supports this and Siu et al. postulated a progressive fading of MT's results due to a possible continued vocal fold atrophy along the years after in-depth review of the literature [4]. Moreover, Hogikyan's (et al.) results seem to support this hypothesis in terms of Voice-related Quality of Life. [8].

The results of this study, however, strongly support the hypothesis that from the patient's perspective, MT, in this case performed with the MTIS, offers a stable voice improvement over the years. MTIS results did not deteriorate over time and were independent of patient's age and gender, prosthesis size and side. The postulated effect of muscle atrophy does not appear to be an issue. Whether this remarkably stable benefit can be called *permanent* remains a rather semantic debate.

This is the largest study assessing the very long term voice results of MTIS from the patient's perspective. Ryu et al. conducted a retrospective study on 40 patients operated for MT with self-carved silicone implants in 2012 [7]. The long-term follow-up was done using acoustic (Jitter, Shimmer) and aerodynamic measures (Mean Airflow Rate and Maximum Phonation Time). Their results were similar, showing stable early and very long term (up to 5 years) post-operative results. They concluded their study by suggesting the launch of further very long term studies on other implants and other voice outcome indicators.

Although the VHI-30 is largely recognized as a valid self-evaluation tool [10], correlation between the subjective VHI-30 and objective acoustic and aerodynamic measures is poor [11-13]. Therefore this patient-centered approach represents a different very long-term assessment method. Considering Ryu's results and the results in this study, a five-year permanency of MT results has now been established using two different research methods (cross-sectional versus retrospective), two different voice assessment approaches (VHI-30 versus acoustic and aerodynamic measures) and with two different types of implants (MTIS and self-carved silicone). Furthermore, this study demonstrates that variables such as age of the patient at the time of surgery, gender and prosthesis characteristics (size and side) do not influence this permanency of results.

The permanency of MT results is of particular interest when it comes to cost minimization analysis and treatment decision making. A recent Canadian study by Tam et al. [14] compared the costs of MTIS versus repeated injection laryngoplasty (IL) with hydroxyapatite. They concluded that, for a similar early (<2 years) effectiveness, IL will offer a cost saving of 596 CA$. However the hydroxyapatite has a lifespan on average of 18 months [15], and with the MT's results now showing evidence of 5 years permanency, the cost/benefit analysis could switch in favor of MT, especially for

patients having a longer life expectancy than 2 years. Further prospective studies should focus on life expectancy of the patients as a surgical decision making determinant.

Some bias and limitations of our study should be taken into consideration. In order to gather enough patients meeting the inclusion criteria, a multi-centric approach was chosen. The way the VHI-30 questionnaires were collected differed for one center. Center 2 invited patients by phone rather than by mail. Center 2's VHI-30 were also filled in within the clinic setting rather than at patients' homes. This modification of data collection was considered more appropriate to the cultural and sociological background of this particular group of patients. Authors acknowledge a possible data collection bias although no statistical differences in very long-term VHI-30 assessments were noted between centers.

Furthermore, although the MTIS procedure is known as an easily reproducible step-wise surgical approach, operative variances in techniques and variations in operative experience between centers might have influenced results. However, one complimentary injection laryngoplasty for unsatisfactory post-MTIS voice result out of 50 surgeries (2%), represents a lower failure rate than the MT failure rates that are published in the literature [16,17]. Therefore we believe that technical variability did not have a large impact on our results.

Finally, as centers 1 and 2 had a response rate above the 80%, and center 3 a response rate of 56%, this difference could also represent a possible bias. We don't have much rationale for this difference of responder's rate except for the fact that some of this center's patients had been operated by a surgeon who left the institution. Some patients of center 3 might have been less motivated by a request for participation signed by an unknown surgeon. Nevertheless, despite this caveat, the overall response rate (78%) was 10% higher that the response rate of Hogikyan et al. (68%)[8] and was thus considered valid for interpretation.

Conclusions

This study shows that MT performed with the MTIS offers permanency of voice improvement from the patient's perspective. Age, gender, side of procedure and size of MTIS implants does not influence very long term results in terms of VHI-30. Therefore, MT overall and MTIS in particular, should be considered as a possible standard of care for UVFP when permanency of voice results is sought.

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