Long-term voice quality outcome after thyroidectomy without laryngeal nerve injury: a prospective 10 year follow up study

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Highlights

- A prospective longitudinal study design was used to investigate the evolution of vocal function in thyroidectomy patients.
- Thyroidectomy without laryngeal nerve injury does not cause a permanent voice change.
- •Progressive amelioration of voice quality was found in patients who underwent thyroidectomy.

Abstract

Purpose: This study investigates the long-term voice outcome of thyroidectomy up to 10 years after the surgery using a longitudinal prospective study design.

Methods: Eighteen participants (6 men and 12 women, mean age: 54 years) who underwent a thyroidectomy between September 2006 and May 2007 were included in this study. A voice assessment protocol consisting of subjective (videolaryngostroboscopic evaluation, auditory- perceptual evaluation, patients' self-report) and objective voice assessments (maximum performance task, acoustic analysis, voice range profile and Dysphonia Severity Index) was used to evaluate the participants' pre- and postoperative voice. Voice measurements were compared before and one week, six weeks, three months and 10 years after the surgery.

Results: No significant differences over time in auditory-perceptual and objective voice parameters were found, except for shimmer. Only in the first postoperative condition, significantly more patients reported vocal complaints. A progressive amelioration of the vocal folds' movement patterns was observed in the postoperative conditions.

Conclusion: The findings of this small longitudinal prospective study suggest that thyroidectomy without laryngeal nerve injury does not cause a permanent deterioration of the laryngeal aspect or function, vocal fold behavior and the self-perceived, perceptual and objective vocal quality. The increase of the shimmer 10 years post-thyroidectomy may be related to vocal aging.

Keywords: Thyroidectomy; laryngology; long-term follow-up; voice quality; voice outcome

1. Introduction

Vocal complaints are frequently reported symptoms after thyroidectomy. Recurrent laryngeal nerve (RLN) palsy (paresis or paralysis) resulting in dysphonia is a known and feared complication in thyroid surgery with an average incidence of 9.8% (Jeannon et al., 2009). A permanent RLN palsy occurs in 2.3% of the thyroidectomy patients (Jeannon et al., 2009). However, even in the absence of a postoperative RLN injury, studies have shown that 25% to 87% of patients complain about voice impairment after thyroidectomy (Sinagra et al., 2004; Hong & Kim, 1997, Stojadinovic et al., 2008; Debruyne et al., 1997; Van Lierde et al., 2010; De Pedro Netto et al., 2006; Lombardi et al., 2009). Possible causes of a post-thyroidectomy voice disorder (PTVD) are operative injury or dysfunction of the prethyroid strap muscles influencing pitch control, postoperative inflammation, laryngotracheal fixation, cricothyroid or cricoarytenoid trauma, perithyroidal external branch of superior laryngeal nerve (EBSLN) injury, neural plexus lesions, modifications of the vascular supply and/or venous drainage of the larynx resulting in mucosal changes, and endotracheal intubation-related trauma (Hong & Kim, 1997; Stojadinovic et al., 2008; Debruyne et al., 1997; Tanaka et al., 2003; McIvor et al., 2000). Additionally, pain, psychological reaction and a loss of general fitness after the surgery can also lead to voice alterations (Debruyne et al., 1997).

The short-term effects of thyroidectomy on the voice characteristics are well described in the literature. In early postoperative stages, up to 87% of the patients report vocal complaints including vocal fatigue, roughness, difficulties with high frequencies and singing, and volume reduction (Sinagra et al., 2004; Hong & Kim, 1997, Debruyne et al., 1997). During the first weeks and months after surgery, acoustic analysis of the voices reveals a deterioration of the acoustic parameters and the vocal quality. The most prominent acoustic changes are a lowering of the habitual fundamental frequency, a reduced frequency and intensity range, and an increase of the different perturbation parameters, such as shimmer, jitter, noise-to-harmonic ratio, and voice turbulence index (Jeannon et al., 2009; Sinagra et al., 2004; Hong & Kim, 1997, Stojadinovic et al., 2008; Debruyne et al., 1997; Debruyne et al., 1997; Van Lierde et al., 2010; De Pedro Netto et al., 2006; Soylu et al., 2007; Musholt et al., 2006; Park et al., 2016). Most acoustic parameters seem to progressively ameliorate over time, indicating that most of the postoperative vocal alterations in the absence of RLN injuries are temporary (Sinagra et al., 2004; Hong & Kim, 1997; Debruyne et al., 1997; Van Lierde et al., 2010; Musholt et al., 2006).

In a retrospective study, Sahli et al. (2019) found that age (≥ 50 years) is independently associated with the development of voice or swallowing changes after thyroidectomy without RLN injury. Papadakis et al. (2017) also found differences in voice outcomes and psychosocial impact between thyroidectomy patients younger and older than 40 years (age at thyroidectomy). Patients younger than 40 years at the age of thyroidectomy showed a significant difference in pitch, maximum phonation time and auditory-perceptual evaluation between pre- and 1 week post-thyroidectomy. Patients older than 40 years at the age of thyroidectomy showed the same postoperative differences and an additional deterioration in noise-to-harmonic ratio and Voice Handicap Index. The evidence and documentation of PTVD has led to the recommendation of the American Thyroid Association to follow up on patients' voice quality by performing pre- and postoperative voice assessments. Especially in older patients, an accurate follow-up of voice alterations is necessary. This follow-up should recognize the multidimensionality of voice by including subjective and objective assessments, and multiparameter indices (Dejonckere et al., 2003; Van Lierde et al., 2010). The Dysphonia Severity Index is such a multiparameter index that have been proven responsive to vocal quality changes (Wuyts et al., 2000).

To date, most research focused on the short-term voice outcome (i.e. several weeks) after thyroidectomy. Only a few studies investigated the longer-term voice outcome, up to one (Musholt et al., 2006; Park et al., 2016, Park et al., 2018; Minni et al., 2014; Borel et al., 2018; Lee et al., 2016; Lee et al., 2017) or two years (Sung et al., 2018) after surgery. In the study of Sung et al. (2018), self-reported voice symptoms and impairment of the vocal range (highest frequencies) continued for more than 18 months. The long-term outcome after more than two years has, to the best of our knowledge, not been investigated using a prospective design. However, knowledge of this long-term outcome is important for clinical practice as patients need to be correctly informed about the postoperative voice. Furthermore, clinicians need to know whether a reported history of thyroidectomy is a meaningful incident that might influence the results of a voice assessment. Therefore, the purpose of this study was to investigate the long-term impact of thyroidectomy on subjective and objective voice characteristics by comparing the preoperative and short-term postoperative outcomes published in a previous article (Van Lierde et al., 2010) with the postoperative outcome after 10 years.

2. Methods

2.1. Participants

The study was approved by the ethical committee of Ghent University Hospital (Belgian registration numbers: B670201733815, B670201733817). Forty-four participants of the previous study (Van Lierde et al., 2010), who underwent a thyroidectomy between September 2006 and May 2007, were invited to participate in the current study. They were all contacted by telephone in 2017. Of the 44 participants, two had died, two were in poor health condition and 22 did not want to participate in this long-term follow-up study or were not reachable. The final group consisted of 18 participants, 6 men and 12 women with a mean age of 54 years (range: 28-76 years). An overview of the characteristics of the participants is presented in Table 1.

Table 1. Characteristics of the Participants.

	M (range)	
Age		
Men	54.3 yrs. (28-76 yrs.)	
	Women	53.8 yrs. (41-74 yrs.)
	n (%)	
Sex		
	Men	6/18 (33)
	Women	12/18 (67)
type of voice user		
	Professional voice users	3/18 (17)
	Non-vocal professionals	10/18 (55)
	Non-vocal non-professionals	5/18 (28)
Type of thyroidectomy		
Total thyroidectomy	14/18 (78)	
Hemi thyroidectomy	4/18 (22)	
Medical indication		
	Multinodular struma	12/18 (67)
	Graves' disease	1/18 (5.5)
	Papillar carcinoma	1/18 (5.5)
	Follicular carcinoma	1/18 (5.5)
	Nodules	1/18 (5.5)
	Cysts	1/18 (5.5)
	Follicular adenoma	1/18 (5.5)
Voice risk factors		
	Vocal misuse	10/18 (56)
	Nasal obstruction	7/18 (39)
	Smoking	3/18 (17)
	GER	1/18 (6)
	Allergy	2/18 (11)
	COLD	1/18 (6)
	URT infection	3/18 (17)
	Vocal fatigue	9/18 (50)

Note. GER: gastroesophageal reflux, COLD: chronic obstructive lung disease, URT: upper respiratory tract.

Professional voice users: voice users for whom a moderate vocal difficulty hampers adequate job performance. Non-vocal professionals: professionals who can perform their job with slight or moderate (but no severe) voice problems. Non-vocal non-professionals: people who are not impeded from doing their work when they experience any kind of dysphonia (Koufman & Isaacson, 1991).

2.2. Surgical procedure

All participants were operated on by the same head and neck surgeon (H.V.) and with the same surgical technique. After the evaluation by the endocrinologist, either a a total thyroidectomy or hemithyroidectomy was performed (seeVan Lierde et al. (2010) for description).

2.3. Voice assessments

A standardized voice assessment consisting of subjective (videolaryngostroboscopic evaluation, auditory-perceptual evaluation, patients' self-report) and objective (maximum performance task, voice range profile, acoustic analysis, Dysphonia Severity Index (DSI)) vocal measures was used to evaluate the participants' voices. Identical procedures for the voice assessment were used before thyroidectomy and one week, six weeks, three months and 10 years postoperative. Assessments were performed by three speech-language pathologists (SLPs) (E.D., L.S., O.V.) and the data were analyzed by the same SLP with 14 years of expertise in voice (E.D.) (at the moment of the current long-term follow-up study) in a sound-treated room at Ghent University Hospital.

2.3.1. Videolaryngostroboscopic evaluation

Videolaryngostroboscopy was performed by head and neck surgeons (H.V. and W.H.) using a standardized protocol (Remacle et al., 1996). In the preoperative and first three postoperative examinations, a Karl Storz 90° rigid endoscope (Germany, model 8704D-90°) and a stroboscope of Stroboview 2000 (Alphatron Medical Systems, Rotterdam) was used. In the last postoperative assessment, a flexible scope (Pentax Medical High Definition Digital Video Capture Module: Model 9310HD) was used. Laryngeal aspect and function (symmetry, regularity, glottal closure, and mucosal wave) were randomly and blindly evaluated by the same experienced SLP (E.D) at each time point using the procedure of Remacle et al. (1996). To assure interrater reliability, 50% of the samples were judged at random, blindly and independently, by another SLP with six years of experience in voice diagnostics (I.M.).

2.3.2. Auditory-perceptual evaluation

The perceptual voice quality was evaluated using the GRBAS scale (Hirano et al., 1981). The GRBAS consists of five well-defined parameters: G (overall grade of hoarseness), R (roughness), B (breathiness), A (asthenia) and S (strain) of the voice. A sixth parameter I (Dejonckere et al., 1996) for instability of the voice was added to the GRBAS scale. A four-point grading scale (0 = normal, 1 = slight, 2 = moderate, 3 = severe) was used for each parameter. The voice samples of connected speech were video and audio recorded [Sony DAT 55ES (Sony Corp., Tokyo, Japan)] for further analysis. Voice samples were randomized and presented blindly to the same experienced SLP (E.D.). Fifty percent of the samples were judged at random, blindly and independently, by another SLP experienced in voice diagnostics (I.M.) to determine the interrater reliability.

2.3.3. Questionnaires

Participants' history for voice influencing factors was investigated using the questionnaire of the European Laryngological Society (ELS) protocol (Dejonckere et al., 2001). To measure the psychosocial impact of vocal complaints, the Dutch version (De Bodt et al., 2000) of the Voice Handicap Index (VHI) (Jacobson et al., 1997) was used. The VHI is a self-rating questionnaire consisting of 30 statements evaluating functional, physical, and emotional restrictions. Every statement is evaluated on a 5 point Likert scale. The total VHI score varies between 0 and 120 with higher scores indicating more self-perceived disability due to voice difficulties.

2.3.4. Objective vocal measurements

2.3.4.1. Maximum performance task

The maximum phonation time (MPT) for the sustained vowel /a:/ was measured in seconds after a maximal inspiration at the participants' habitual loudness and pitch in sitting position and in free field (free from sound reflections and without a microphone). All participants received verbal and visual encouragement and coaching. The best value of two test trials was retained for further analysis.

2.3.4.2. Voice Range Profile

The frequency and intensity range were measured using a Shure SM-48 microphone located at a distance of 15 cm from the mouth, angled at 45 degrees, and the Computerized Speech Lab (CSL, model 4500, KayPENTAX, Montvale, NY). The procedure of Heylen et al. (1998) was used to determine the lowest and highest fundamental frequency (F-low and F-high), and the lowest and highest intensity (I-low and I-high). Participants were instructed to produce the vowel /a:/ for at least 2 seconds using, respectively, a habitual pitch and loudness, a minimal pitch, a minimal intensity, a maximal pitch, and a maximal intensity. Voice productions were modeled by the experimenter and the participants received visual and verbal encouragement.

2.3.4.3. Acoustic analysis

An acoustic analysis of the sustained vowel /a:/ was performed using the Multidimensional Voice Program (MDVP) of the CSL using a sampling rate of 50 000Hz. The participants were instructed to produce the vowel /a:/ at habitual speaking pitch and loudness. A midvowel segment of 3 seconds was retained for further analysis. The following acoustic parameters were analyzed: fundamental frequency (f_0 in Hz), amplitude tremor intensity index (Atri in %), frequency tremor intensity index (Ftri in %), jitter (%) and shimmer (%),

2.3.4.4. Dysphonia Severity Index (DSI)

The DSI is a multiparameter approach designed to establish an objective and quantitative correlate of the perceived vocal quality (Wuyts et al., 2000). The index is based on a weighted combination of the following parameters: MPT (in s), F-high (in Hz), I-low (in dB) and jitter (in %). The index is constructed as 0.13 MPT + 0.0053 F-high − 0.26 I-low − 1.18 jitter + 12.4 and ranges from -5 to +5 for severely dysphonic to normal voices. A more negative index indicates a worse vocal quality. The threshold separating normophonic from dysphonic persons is 1.6 (Raes et al., 2002). The DSI can be calculated as a percentage by increasing the value with five points and then multiplying it by 10 (Raes et al., 2002).

2.4. Statistical analysis

SPSS version 24 (SPSS Corporation, Chicago, IL) was used for the statistical analysis of the data. Analyses were conducted at $\alpha = .05$. Linear mixed models (LMM) were used to compare the data over time on each continuous outcome measure (objective voice measures and VHI), using the restricted maximum likelihood estimation and scaled identity covariance structure. Time was specified as a fixed factor. A random intercept for participants was included. Model assumptions were checked by inspecting whether residuals were normally distributed. Post-hoc pairwise comparisons with Bonferroni correction were used if a significant time effect was found. For the variables f_0, Fhigh and Flow sex was added in the model as a covariate. For the comparison of the ordinal data (GRBASI) over time, the non-parametric Friedman test with Dunn-Bonferroni post-hoc tests was used. Cohen's kappa and weighted kappa were run to determine interrater reliability of the videolaryngostroboscopic (nominal) and auditory-perceptual (ordinal) data, respectively.

3. Results

The results of the videolaryngostroboscopic evaluation of the participants of this study before and after thyroidectomy are presented in Table 2. At 10 years post thyroidectomy, a general improvement was observed for all parameters (symmetry, regularity, glottal closure, and mucosal wave) compared to the preoperative and short-term postoperative time points. Substantial degrees of interrater reliability were found for the parameters symmetry and regularity, with κ = .77. Perfect degrees of interrater reliability were found for the parameters glottal closure, type of gap and mucosal wave, with κ = 1.00 (Landis & Koch, 1977).

Table 2. Pre- and Postoperative Videostroboscopic Evaluations.

		pre *n* (%)	post 1 *n* (%)	post 2 *n* (%)	post 3 *n* (%)	post 4 *n* (%)
symmetry	symmetric	8/13 (62)	10/13 (77)	5/6 (83)	2/4 (50)	15/18 (83)
	asymmetric	5/13 (38)	3/13 (23)	1/6 (17)	2/4 (50)	3/18 (17)
regularity	regular	6/12 (50)	3/13 (23)	2/6 (33)	2/4 (50)	11/18 (61)
	irregular	5/12 (42)	9/13 (69)	4/6 (67)	0/4 (0)	6/18 (33)
	inconsistent	1/12 (8)	2/13 (15)	0/6 (0)	2/4 (50)	1/18 (6)
glottic closure	complete	7/13 (54)	9/15 (60)	3/6 (50)	2/4 (50)	12/18 (67)
	incomplete	6/13 (46)	6/15 (40)	3/6 (50)	2/4 (50)	6/18 (33)
	inconsistent	0/13 (0)	0/15 (0)	0/6 (0)	0/4 (0)	0/18 (0)
type of gap	longitudinal	3/6 (50)	1/6 (17)	0/3 (0)	0/2 (0)	0/6 (0)
	posterior	0/6 (0)	2/6 (33)	0/3 (0)	0/2 (0)	3/6 (50)
	anterior	1/6 (17)	0/6 (0)	0/3 (0)	0/2 (0)	1/6 (17)
	irregular	2/6 (33)	1/6 (17)	2/3 (67)	1/2 (50)	2/6 (33)
	oval	0/6 (0)	1/6 (17)	0/3 (0)	0/2 (0)	0/6 (0)
	hourglass	0/6 (0)	1/6 (17)	1/3 (33)	1/2 (50)	0/6 (0)
mucosal wave	normal	5/12 (42)	9/14 (64)	3/6 (50)	1/4 (25)	16/18 (89)
	reduced	7/12 (58)	5/14 (36)	3/6 (50)	3/4 (75)	2/18 (11)
	non	0/12 (0)	0/14 (0)	0/6 (0)	0/4 (0)	0/18 (0)

Note. pre: before thyroidectomy, post 1: 1 week after thyroidectomy, post 2: 6 weeks after thyroidectomy, post 3: 3 months after thyroidectomy, post 4: 10 years after thyroidectomy

Table 3 shows the results of the auditory-perceptual evaluations using the GRBASI scale. Ten years postoperative, the voice was perceptually rated between normal and slightly deviant (mean ratings: G0.4 R0.4 B0.1 A0.2 S0.2 I0.1). No significant differences in perceptual evaluation were observed between the pre- and postoperative conditions, except for the parameter R (Friedman test, $\chi^2(2) = 6.686$, $p = .035$). Substantial degrees of interrater reliability were found for the parameters G, R and S, with κ = .77, κ = .77 and κ = .73, respectively. Perfect degrees of interrater reliability were found for the parameters B, A and I, with κ = 1.00 (Landis & Koch, 1977).

Table 3. Pre- and Postoperative Auditory Perceptual Evaluations.

n=18		M	Mdn	SD	Min	Max	Friedman test χ^2	*p*
G	pre	0.4	0	0.5	0	1.5		
	post 1	0.5	0.5	0.5	0	1.5		
	post 4	0.4	0.5	0.4	0	1	4.187	.123
R	pre	0.3	0	0.4	0	1		
	post 1	0.6	0.5	0.4	0	1.5		
	post 4	0.4	0.5	0.4	0	1	6.686	.035*
B	pre	0.1	0	0.3	0	1		
	post 1	0.1	0	0.3	0	1		
	post 4	0.2	0	0.4	0	1	0.421	.810
A	pre	0.2	0	0.4	0	1		
	post 1	0.2	0	0.4	0	1		
	post 4	0.2	0	0.4	0	1	1.000	.607
S	pre	0.2	0	0.4	0	1.5		
	post 1	0.2	0	0.4	0	1		
	post 4	0.2	0	0.4	0	1	0.087	.957
I	pre	0.1	0	0.4	0	1.5		
	post 1	0.3	0	0.5	0	1.5		
	post 4	0.0	0	0.1	0	0.5	4.957	.084

Note. G: grade, R: roughness, B: breathiness, A: asthenia, S: strain, I: instability

pre: before thyroidectomy, post 1: 1 week after thyroidectomy, post 4: 10 years after thyroidectomy

∗indicates a significant effect ($p < .05$)

Vocal complaints inventoried using the ELS protocol are shown in Fig. 1. In the preoperative condition, 22% (n=4/18) of the participants reported vocal complaints with roughness as the most frequently reported symptom (n=3/18, 17%). The highest number of participants reporting vocal complaints was found in the first postoperative condition (n=12/18, 67%). In the second and third postoperative condition, the participants with vocal complaints decreased respectively to 58% (n=7/12) and 25% (n=2/8). Ten years postoperative the number of participants with vocal complaints slightly increased to 33% (n=6/18).

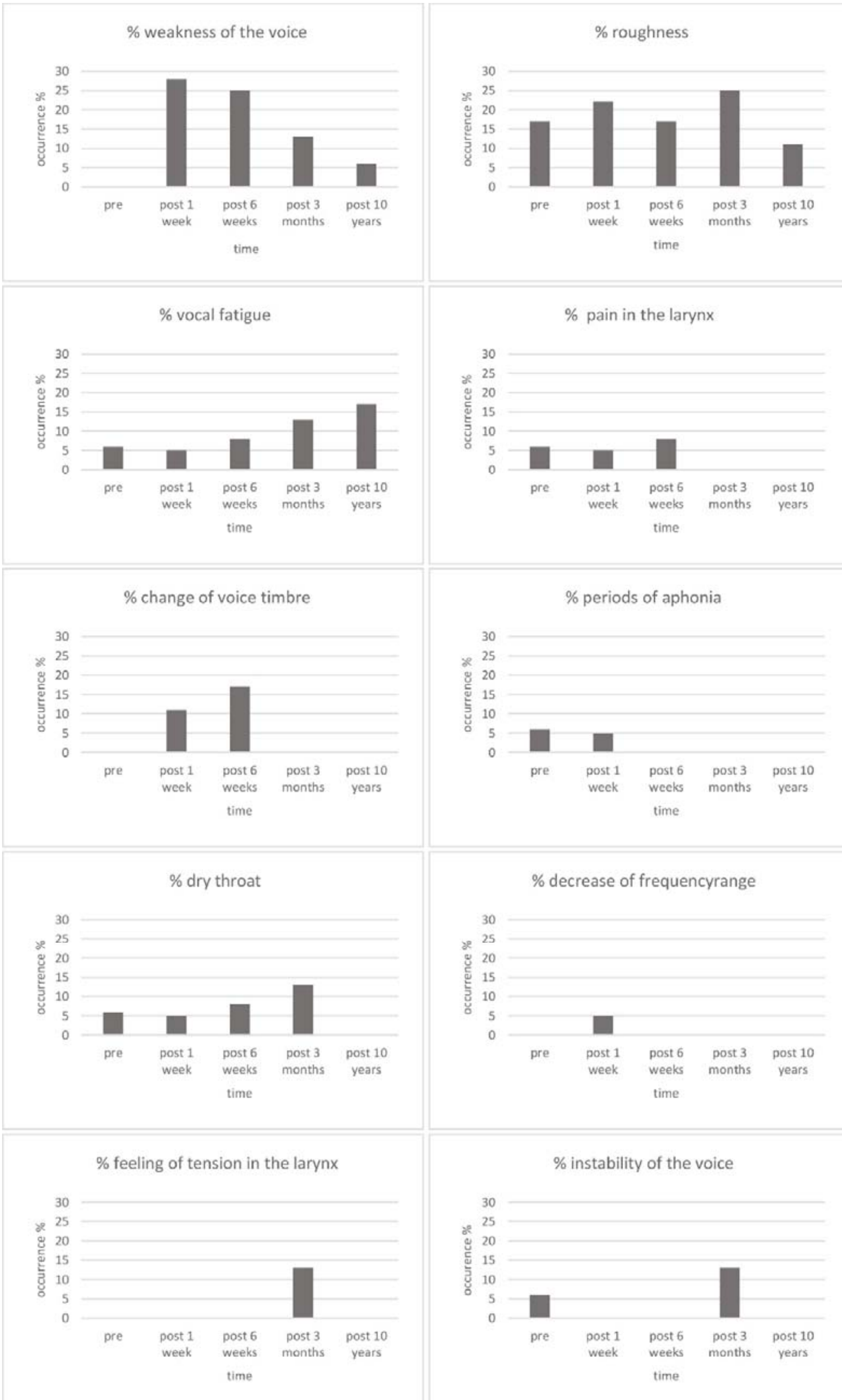

Fig. 1. Number of patients (%) reporting vocal complaints in pre- and post-thyroidectomy evaluations.

The results of the pre- and postoperative objective voice assessments and the VHI are presented in Table 4. For f_0, Fhigh and Flow the data are presented separately for male and female participants (Table 5). No significant differences in objective voice parameters over time were found, except for the parameter shimmer (LMM, $F(4) = 6.896$, $p < .001$). Pairwise post-hoc comparisons with Bonferroni correction showed a significant higher shimmer 10 years postoperative compared to the preoperative condition (mean difference: 1.8, $p < .001$) and the second (6 weeks) postoperative condition (mean difference: 1.7, $p = .001$). No significant differences were found between the last (10y) and the first (1 week) and third (3 months) postoperative condition (resp. $p = .061$ and $p = .079$). The results of the total VHI score remained stable over time (LMM, $F(4) = .385$, $p = .818$) which is presented in Fig. 2. Unstandardized effect sizes are measured by providing the estimated mean differences and 95% confidence intervals for the outcome variables. The effect sizes are presented in Table 6.

Table 4. Pre- and Postoperative Objective Voice Parameters and Voice Handicap Index.

	Pre			Post 1			Post 2			Post 3			Post 4			LMM
	n	EM	95% CI	*n*	EM	95% CI	*n*	EM	95% CI	*n*	EM	95% CI	*n*	EM	95% CI	*p*
MPT	18	21.1	(17.3, 24.9)	18	21.1	(17.4, 24.9)	12	20.3	(16.0, 24.7)	8	22.8	(17.8, 27.9)	18	20.5	(16.8, 24.3)	.913
VRP																
F-low	18	114.5	(97.9, 131.2)	18	112.9	(96.3, 129.6)	12	123.3	(105.9, 140.6)	8	110.3	(91.9, 128.7)	18	123.2	(106.5, 139.9)	.069
F-high	18	682.4	(595.1, 769.7)	18	644.5	(557.2, 731.8)	12	697.8	(604.4, 791.1)	8	697.0	(595.3, 798.7)	18	659.4	(572.1, 746.7)	.527
I-low	18	59.8	(57.1, 62.6)	18	60.1	(57.3, 62.9)	12	60.8	(57.4, 64.1)	8	58.7	(54.6, 62.8)	18	61.3	(58.5, 64.0)	.827
I-high	18	103.2	(100.0, 106.4)	18	99.3	(96.2, 102.5)	12	103.0	(99.2, 106.7)	8	105.2	(100.7, 109.7)	18	103.9	(100.7, 107.1)	.079
MDVP																
f_0	18	167.4	(143.9, 190.9)	18	165.5	(142.0, 189.0)	12	173.9	(149.8, 198.0)	8	167.0	(142.0, 192.0)	17	164.5	(143.0, 190.0)	.729
Atri	15	2.8	(1.8, 3.8)	15	3.5	(2.5, 4.4)	10	3.4	(2.2, 4.7)	7	3.5	(2.1, 5.0)	11	4.1	(3.0, 5.3)	.548
Ftri	17	0.3	(0.0, 0.7)	17	0.4	(0.1, 0.8)	11	0.9	(0.5, 1.4)	8	0.4	(0.0, 0.9)	16	0.6	(0.2, 1.0)	.288
Jitter	18	1.0	(0.6, 1.5)	18	1.3	(0.9, 1.7)	12	1.3	(0.8, 1.7)	8	1.2	(0.7, 1.8)	17	1.2	(0.8, 1.6)	.777
Shimmer	18	2.2	(1.4, 3.1)	18	3.0	(2.1, 3.8)	12	2.3	(1.4, 3.2)	8	2.7	(1.6, 3.7)	17	4.0	(3.2, 4.9)	<.001*
DSI	18	2.1	(1.0, 3.2)	18	1.5	(0.5, 2.6)	12	1.1	(0.0, 2.3)	8	1.4	(0.0, 2.7)	18	1.5	(0.4, 2.5)	.519
VHI	18	8	(3, 12)	18	9	(4, 13)	12	6	(1, 11)	8	6	(0, 12)	18	7	(2, 12)	.818

Note. MPT: maximum phonation time, VRP: voice range profile, F-low: lowest fundamental frequency, F-high: highest fundamental frequency, I-low: lowest intensity, I-high: highest intensity, MDVP: multidimensional voice program, f_0: fundamental frequency, Atri: amplitude tremor intensity index, Ftri: frequency tremor intensity index, DSI: Dysphonia Severity Index, VHI: Voice Handicap Index

EM: estimated mean, CI: confidence interval, LMM: linear mixed models

pre: before thyroidectomy, post 1: 1 week after thyroidectomy, post 2: 6 weeks after thyroidectomy, post 3: 3 months after thyroidectomy, post 4: 10 years after thyroidectomy

$*p < .05$

Table 5. Pre- and Postoperative lowest, highest and fundamental frequency for male and female participants.

		pre			post 1			post 2			post 3			post 4		
		EM	95% CI		EM	95% CI		EM	95% CI		EM	95% CI		EM	95% CI	
Flow	Women	131.3	116.5	146.1	131.9	117.1	146.7	142.6	126.7	158.5	127.5	108.6	146.4	144.6	129.8	159.4
	Men	81.0	74.3	87.7	74.9	68.2	81.7	83.1	73.5	92.6	76.8	67.3	86.4	80.5	73.7	87.2
Fhigh	Women	744.1	653.9	834.4	714.7	624.4	805.0	777.6	680.4	874.8	789.1	672.2	905.9	696.5	606.2	786.8
	Men	558.8	397.4	720.3	504.2	342.8	665.7	510.4	344.8	675.9	524.3	358.8	689.9	585.1	423.6	746.6
f_0	Women	196.5	181.9	211.2	197.2	182.6	211.9	206.1	190.2	222.0	194.3	175.0	213.6	191.4	176.4	206.4
	Men	109.1	95.4	122.8	101.9	88.3	115.6	104.4	87.7	121.1	113.2	96.6	129.9	115.8	102.1	129.4

EM: estimated mean, CI: confidence interval

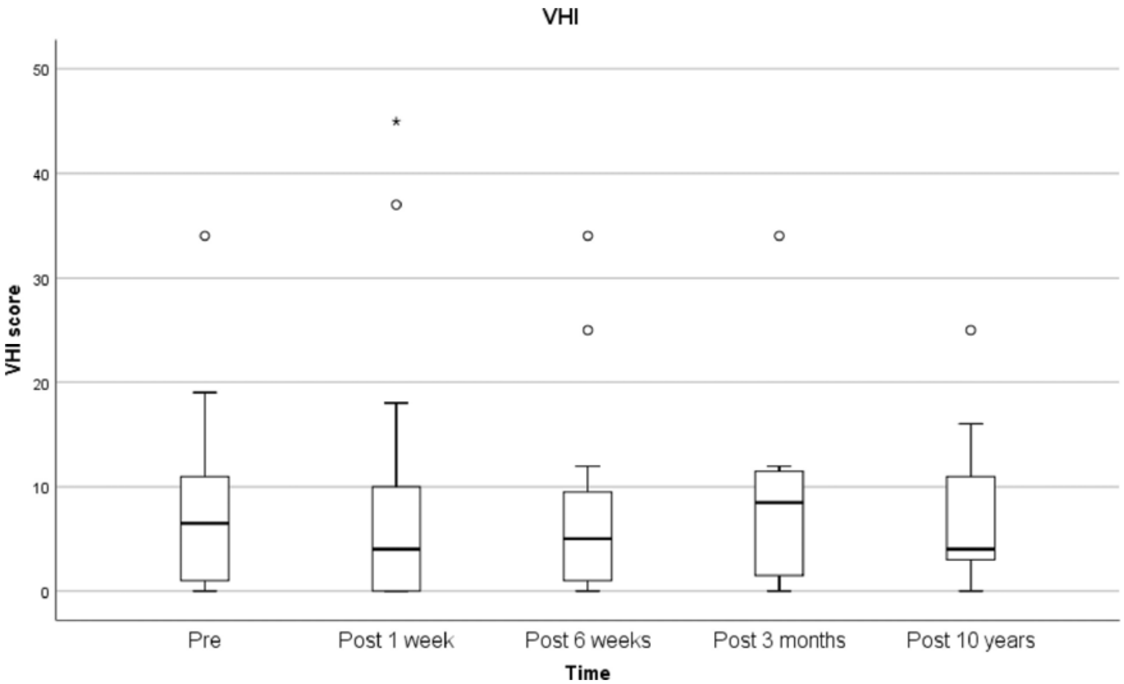

Fig. 2. Box plots of VHI scores in the pre- and post-thyroidectomy evaluations.

Table 6. Effect sizes of the LMM analysis.

		EMD	95% CI		*p*
MPT					
pre	post 1	-0.027	-5.78	5.726	1.000
	post 2	0.755	-5.812	7.322	1.000
	post 3	-1.72	-9.324	5.883	1.000
	post 4	0.559	-5.194	6.312	1.000
F-low					
pre	post 1	1.628	-12.1	15.357	1.000
	post 2	-8.71	-24.502	7.081	1.000
	post 3	4.228	-14.129	22.585	1.000
	post 4	-8.653	-22.382	5.075	.703
F-high					
pre	post 1	37.842	-52.373	128.057	1.000
	post 2	-15.378	-119.002	88.246	1.000
	post 3	-14.619	-134.993	105.755	1.000
	post 4	23.008	-67.207	113.223	1.000
I-low					
pre	post 1	-0.278	-5.552	4.997	1.000
	post 2	-0.954	-6.905	4.997	1.000
	post 3	1.113	-5.726	7.952	1.000
	post 4	-1.444	-6.719	3.83	1.000
I-high					
pre	post 1	3.889	-1.595	9.373	.426
	post 2	0.252	-5.978	6.481	1.000
	post 3	-1.995	-9.187	5.197	1.000
	post 4	-0.667	-6.151	4.817	1.000
f_0					
pre	post 1	1.895	-13.285	17.076	1.000
	post 2	-6.476	-23.957	11.006	1.000
	post 3	0.367	-19.979	20.712	1.000
	post 4	0.894	-14.562	16.351	1.000
Atri					
pre	post 1	-0.649	-2.707	1.409	1.000
	post 2	-0.634	-2.934	1.667	1.000
	post 3	-0.741	-3.321	1.838	1.000
	post 4	-1.331	-3.568	0.906	0.872
Ftri					
pre	post 1	-0.114	-0.847	0.62	1.000
	post 2	-0.607	-1.44	0.226	.374
	post 3	-0.071	-0.999	0.857	1.000
	post 4	-0.235	-0.981	0.511	1.000

Jitter					
pre	post 1	-0.261	-0.896	0.375	1.000
	post 2	-0.252	-0.977	0.474	1.000
	post 3	-0.181	-1.021	0.66	1.000
	post 4	-0.134	-0.78	0.513	1.000
Shimmer					
pre	post 1	-0.712	-1.794	0.371	.593
	post 2	-0.023	-1.263	1.216	1.000
	post 3	-0.409	-1.848	1.029	1.000
	post 4	-1.785	-2.886	-0.684	0.000
DSI					
pre	post 1	0.578	-0.93	2.086	1.000
	post 2	0.989	-0.736	2.714	.991
	post 3	0.733	-1.267	2.732	1.000
	post 4	0.622	-0.886	2.13	1.000
VHI					
pre	post 1	-0.778	-6.862	5.306	1.000
	post 2	1.525	-5.446	8.495	1.000
	post 3	2.014	-6.073	10.102	1.000
	post 4	0.611	-5.473	6.695	1.000

EMD: Estimated Mean Difference

CI: Confidence Interval

4. Discussion

This study was the first to investigate the long-term voice-related outcome of thyroidectomy, 10 years after surgery in patients without laryngeal nerve injury using a prospective study design. The short-term impact of thyroidectomy in these patients was investigated in 2007 (Van Lierde et al., 2010). An identical voice assessment by the same research team was performed 10 years later in 18 of the 44 original participants. This corresponds with a response rate of 41% which is acceptable for a long-term term follow-up after 10 years (Ryu et al., 2012; Van Lierde et al., 2007).

Short-term outcome

In the short-term outcome study (Van Lierde et al., 2010), a significant decrease in f_0, frequency and intensity range and overall voice quality (measured by the DSI) was found in the first postoperative condition (one week after surgery) with a progressive amelioration and normalization of these parameters in the following months (6 weeks and 3 months postoperative). No significant differences in voice parameters were found between total and hemithyroidectomy patients in the study of Van Lierde et al. (2010). The chance for postoperative voice disorders was minimized by specific efforts during surgery such as elaborate hemostasis and careful dissection of the laryngeal nerve, and preservation of the specific muscles important for normal voice production (i.e., the sternohyoid, sternothyroid and omohyoid muscles) (Van Lierde et al., 2010). Three months postoperative, 18% (3/17) of the participants still reported vocal complaints with roughness (12%, 2/17) and vocal fatigue (12%, 2/17) as the most prominent vocal symptoms (Van Lierde et al., 2010). The number of participants reporting vocal complaints was lower compared to the preoperative condition (23%, 10/44) but still higher compared to the general population (3-9%) (Ramig et al., 1998, Roy et al., 2005).

Long-term outcome

Studies investigating long-term outcome are necessary to investigate the presence of long-term voice impairment after thyroidectomy to be able to inform patients of it preoperatively (Sung et al., 2018). Despite the clinical relevance, the long-term voice outcome of thyroidectomy remained unclear. Sung et al. (2018) were the first to investigate the vocal characteristics up to two years after thyroidectomy and concluded that self-assessed voice symptoms and effects on objective acoustic parameters can persist up to 18 months postoperative. The results of this 10 year follow-up study showed no significant differences in perceptual and objective voice parameters, except for the parameter shimmer. The mean overall vocal quality, measured by means of the DSI (and DSI%) remained stable with rather small fluctuations in mean scores from +2.1 (71%) in the preoperative condition to +1.5 (65%), +1.1 (61%), +1.4 (64%) in the short-term postoperative conditions and to +1.5 (65%) in the long-term follow-up after 10 years. The DSI quantifies perceived vocal quality objectively and is designed to detect small changes in vocal quality (Wuyts et al., 2000). On the contrary, for the perceptual assessment the median values for GRBASI were low and varied between 0 and 0.5 in the pre and postop measurements indicating a possible ceiling effect. In all post-thyroidectomy conditions, the mean DSI score was located below the cut-off point of 1.6 (66%) separating normal from dysphonic voices. This borderline DSI also corresponds to the auditory-perceptual ratings of a normal to slightly deviant voice. A significant difference over time was found for the acoustic parameter shimmer. The shimmer deteriorated in the long-term post-thyroidectomy condition compared to the preoperative and the second postoperative condition (6 weeks after surgery). Shimmer is an amplitude perturbation measure and seem to be related to the perceived overall grade of dysphonia and breathiness (Dejonckere et al., 1996). Shimmer values did not change in the first short-term follow-up measurements. This implies that the deterioration of the shimmer after 10 years is either a delayed effect of the surgery, or a consequence of aging. The latter hypothesis is most likely since higher shimmer values are also reported as a characteristic of vocal aging (Ramig et al., 2001; Lortie et al., 2015; Schaeffer et al., 2015). Nevertheless, it is unclear why other acoustic parameters, such as jitter, did not deteriorate as this might also be associated with vocal aging (Ramig et al., 2001; Lortie et al., 2015). To date, more robust acoustic measurements (e.g. cepstral peak prominence) or acoustic multiparameter approaches (e.g. the Acoustic Voice Quality Index) exist to quantify perceived roughness and breathiness (Maryn et al., 2010). However, the strength of this study can be found in the identical voice assessment procedures in the pre- and post-measurements over a period of 10 years.

A clear difference in participants reporting vocal complaints was found over time. The highest number of participants reporting vocal complaints was found one week post-thyroidectomy (n=12/18, 67%). In the next postoperative weeks, the participants with vocal complaints decreased respectively to 58% (n=7/12) after 6 weeks and 25% (n=2/8) after 3 months. Ten years postoperative, the number of participants with vocal complaints slightly increased to 33% (n=6/18). Again, a vocal aging effect might be one hypothesis for this subtle increment. However, it should be taken into account that only half of the participants were present at the 3 months compared to the 10 years follow-up condition, which might have influenced these proportions and interpretations. Compared to the prevalence of vocal complaints in the general population, the presence is relatively high in the pre- as well as the post-thyroidectomy conditions. These results are in accordance with the study of Sung et al. (2018) that compared the voice outcomes of thyroidectomy and parotidectomy and found higher voice symptoms scores in the preoperative as well as the postoperative conditions in the thyroidectomy group. The exact cause of preoperative voice complaints in patients undergoing thyroidectomy is unknown and can possibly be related to compressive symptoms of thyroid nodule, reflux or psychological attitude (Sung et al., 2018, Holler et al., 2014, Sorensen et al., 2014).

Contradictory to the results of the perceptual and objective voice assessment, an in-depth analysis of the videolaryngostroboscopic evaluations 10 years post-thyroidectomy revealed an improvement of the symmetry and regularity of the vocal fold vibration, the glottal closure and the mucosal wave compared to the pre- and short-term postoperative conditions. A week after surgery, regularity of the vocal fold vibration was clearly diminished. De Pedro Netto et al. (2006) also showed short-term postoperative laryngeal alterations in 28% of the thyroidectomized patients. The improving results of the vocal folds' movement patterns after 10 years are surprising because it is known that with aging, both the periodicity, symmetry, and amplitude of vibration reduce (Biever et al., 1989, Pontes et al., 2006). However, one should take into account that for the laryngostroboscopic evaluation different instruments were used in the short- (rigid scope) and long-term (flexible scope) follow-up study. Moreover, during the short-term measurements missing data due to a gag reflex provoked by the rigid laryngoscope may have influenced the outcome results. Future research on a larger sample of stroboscopic data is necessary to perform a reliable statistical analysis.

Limitations of the study

This study has its limitations. Laryngeal electromyography was not performed to exclude EBSLN paralysis definitively. However, videolaryngostroboscopic examinations showed no evidence of EBSLN paralysis in any of the participants. A control group of participants undergoing another type of surgery is lacking in this study. Although a response rate of 41% 10 years after the surgery is acceptable, the sample size is relatively small and the lack of information of the remaining 26 participants might have influenced the results. The voice assessments and the instruments were identical in all conditions except for the laryngoscopy. After 10 years the rigid stroboscope was replaced by a flexible scope. The same experimenters performed the assessments and auditory perceptual and videostroboscopic ratings were randomized and performed by blinded assessors. For the objective measurements and analysis the CSL was used. However, even in objective assessments a risk for experimenter bias is present because the assessors were not blind for the time point of the measurements. Another limitation of the study is the heterogeneity in type of thyroidectomy (4 hemi versus 14 total). It can be hypothesized that removing the entire thyroid gland is associated with a higher risk for vocal impairment than removing half of it. In a study of Lee et al. (2016), DSI scores deterioration postoperatively was only seen in patients undergoing a total thyroidectomy, not those undergoing a hemithyroidectomy. The study of Van Lierde et al. (2010), on the contrary, showed no significant differences in outcome parameters between these two types of thyroidectomy. Statistical comparison in the current study is difficult because of the small group of hemithyroidectomy patients. In future studies, comparison of the long-term voice outcome at different time points between a larger groups of total and hemilaryngectomy patients with different etiology should be performed to gain more insight in this heterogeneous thyroidectomy population.

5. Conclusions

The findings of this small longitudinal prospective study suggest that thyroidectomy without RLN injury does not cause a permanent deterioration of the laryngeal aspect or function, vocal fold behavior, and the self-perceived, perceptual or objective vocal quality. An increase of the acoustic parameter shimmer was found 10 years post-thyroidectomy which can possibly be related to vocal aging. The results of this study are important for clinical practice as patients need to be correctly informed about the postoperative voice outcome. Furthermore, clinicians need to know whether a reported history of thyroidectomy is a meaningful incident that might influence the results of a voice assessment.

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Concepts of the study	x	x	x					x
Design of the study	x	x	x					x
Definition of intellectual content	x	x						x
Literature search	x			x		x	x	x
Data acquisition	x	x	x			x	x	
Statistical analysis and interpretation of the data	x			x	x	x	x	
Drafting of the manuscript	x	x		x				
Critical revision of the manuscript for important intellectual content	x	x		x	x			
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