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Voice quality, vocal performance and swallowing ability in early laryngeal cancer patients; a comparison before and after cancer treatment.

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Contents

Abstract - 4 -

1. Theoretical framework - 5 -
   1.1. Introduction
   1.2. Evaluation of laryngeal functioning and health-related quality of life
      1.2.1. Evaluation of voice quality
      1.2.2. Evaluation of swallowing function
      1.2.3. Patients perception of health-related quality of life
   1.3. Functional outcome in early laryngeal cancer
      1.3.1. Pre-treatment voice characteristics and vocal functioning
      1.3.2. Voice characteristics and vocal functioning after laser surgery
      1.3.3. Voice characteristics and vocal functioning after radiotherapy
      1.3.4. Pre- and post-treatment swallowing function

2. Objectives, hypothesis and research question - 10 –
   2.1. Objectives
   2.2. Hypothesis
   2.3. Research questions

3. Method - 12 -
   3.1. Participants
   3.2. Procedure
   3.3. Materials
   3.4. Analysis
      3.4.1. Acoustic analysis
      3.4.2. Statistical analysis

4. Results - 14 -
   4.1. Patient characteristics
   4.2. Baseline characteristics
      4.2.1. Pre-treatment voice characteristics
      4.2.2. Pre-treatment self-perception of health-related quality of life
   4.3. Comparison baseline and one-year follow-up
      4.3.1. Alterations in voice characteristics

4.3.2. Correlations of acoustic parameters
4.3.3. Alterations in self-perception of health-related quality of life
4.3.4. Correlations of health-related quality of life parameters
4.3.5. Correlations of acoustic and health-related quality of life parameters

5. Discussion - 21 -
5.1. Discussion of the results
5.1.1. Voice characteristics, vocal performance, and swallowing ability outcomes in perspective
5.1.2. Correlations of outcome measurements in perspective
5.2. Limitations and strengths of the study

6. Conclusion - 26 -
6.1. Synopsis of key findings
6.2. Recommendations

References - 28 -

Abstract

Objectives. Advancement in early laryngeal cancer management led to excellent tumor control. Secondary outcomes such as voice quality and health-related quality of life are of growing importance. Purpose of this study was to investigate voice quality and patients based experiences on vocal functioning and swallowing ability before and after treatment.

Study design. A prospective controlled study is conducted including twenty patients who were treated for small laryngeal carcinoma (≤T3). Patients were assessed before and ≥12 months after treatment.

Methods. Fourteen patients were treated with CO_2 laser surgery, six patients received radiotherapy. Vocal performance is made objective with audio recordings of a read aloud text and a sustained vowel /a/. Self-perception of voice and swallowing problems are surveyed. Acoustic analysis is performed using Praat software. Statistical analysis is performed using SPSS by means of the independent t-test, Welch's t-test and Pearson's correlation coefficient.

Results. Before treatment, a significantly larger impact on self-reported voice functioning is found in patients with T1 staged tumors compared to patients with T2 staged tumors ($t(10) = 3.32$, $p = .008$). After treatment patients with T1 staged tumors show an improvement in vocal functioning compared to patients with T2 staged tumors where deterioration is seen (VHI; $t(7)= -3.60$, $p = .009$). No significance is found for the acoustic analyses and for the questionnaires evaluating swallowing problems. Wide standard deviation values for the acoustic measurements and health-related quality of life values indicate the existence of deviant functioning.
Strong correlations are found between the acoustic parameters, as well as strong correlations between the parameters of the validated health-related quality of life questionnaires. Weak and debatable correlations are found when evaluating the correlations between these two concepts.

Conclusion. The evidence to date shows presence of voice and swallowing problems in the group of early laryngeal cancer patients. Findings of the evaluated studies, this study and future research can lead to recommendations that ensure optimal preservation of function and maximization of health-related quality of life.

1. Theoretical framework

1.1 Introduction

In the group of head and neck squamous cell carcinoma, cancer of the larynx is the most prevalent in Western Europe. (1). In males, a higher incidence of early laryngeal cancer is seen compared to females (36.600-3.800 in Europe in 2008) (2, 3). Usage of tobacco and alcohol are important risk factors for the development of laryngeal cancer (4).

Size, depth and extension of the tumor is classified by t-stages (5). The larynx is divided into three sections. In order of estimated cancer incidence these laryngeal sections are: glottis, supraglottis, and subglottis (6). Because of the frequent involvement of the vocal folds, voice problems is a common manifestation of early laryngeal carcinoma (4, 6, 7). In 56%-75% of the cases, the disease is diagnosed in an early stage (≤T3), most often located at the glottis (6).

For patients with small laryngeal malignancies, CO_2 endoscopic laser surgery (laser surgery) and radiotherapy (RT) have become the treatment modalities of first choice (6). Both options provide high and comparable rates of local control, survival, and functional outcome (8-10). An advantage of laser surgery is the low burden for the patient since it is a one-day treatment. Furthermore, laser surgery can be provided repeatedly or adjuvant RT can be given, in case of recurrent disease (3, 6, 11). On the other hand, laser surgery is an invasive treatment option with increased risks of hemorrhage, infection and granuloma formation (12). An advantage of RT is that there is no need for general anesthesia. However, in RT the period of treatment is much longer and surrounding healthy tissues can be damaged and might suffer from dryness, fibrosis and edema (3, 11, 13). Another disadvantage of RT is that it can be delivered only once at the same target area within a period of five years (11).

Treatment of early stage laryngeal cancer is aimed at laryngeal preservation; key concerns are disease control and post treatment functional outcomes. Patients treated for early stage laryngeal cancer are cured in more than 90% of the cases. This good prognosis highlights the importance of identifying the side effects of the treatment (1, 14). To determine optimal management approach for each patient, functional outcomes and quality of life have to be taken into account (7).

1.2 Evaluation of laryngeal functioning and health-related quality of life

The laryngeal area is involved in the physiological function of breathing, swallowing, and phonation (15). The larynx facilitates respiration and provides a sphincter function to protect the lower airways during the oropharyngeal phase of swallowing. Secondary function of the larynx is its phonatory function (15). Early laryngeal cancer as well as its treatment cause alterations in the anatomy and physiology of the laryngeal system (4). In the following sections evaluation of voice quality, swallowing function and health related quality of life will be further explained

1.2.1 Evaluation of voice quality

Phonation is one of the basic laryngeal functions. Voice is the sound that is produced when the vocal folds adduct and vibrate in a cycling pattern driven by the pulmonary air stream. (16, 17). Voice quality can be assessed by perceptual, acoustic, aerodynamic and stroboscopic methods and trough self-assessment by health-related quality of life (HRQoL) questionnaires (18). For monitoring pathological voice, a multidimensional voice analysis is recommended (18-20). Given that patients perception is a subjective tool, Dejonckere et al. (18) recommend to compare self-reported outcomes with objective assessment.

In this project, acoustic analysis is subject of interest for objective voice evaluation. Acoustic analysis provides an objective, non-invasive and quantitative assessment of voice quality (20, 21). Acoustic voice assessment regularly includes frequency and amplitude measurements (22). Fundamental frequency (F_0), a result of the rate of vibration of the vocal folds, is perceptually related to vocal pitch (23). Perturbation analysis describes the disturbances in the cycle-to-cycle-pattern using frequency and amplitude measurements (24). Jitter refers to the relative variability in the period-to-period frequency, and shimmer refers to the relative variability in the peak-to-peak amplitude (24, 25). These measures provide information about the regularity of the fundamental frequency and consistency of the amplitudes (24, 25). Harmonics to noise ratio (HNR) is the ratio between the total energy of the voice signal and the energy of the noise components (23, 25). HNR parameters are useful to measure the degree of turbulent air escaping through the glottis during phonation. Healthy phonating of the vowel /a/ should have a HNR of 20 (26). HNR values below 20 are considered to be a possible predictor for breathiness and roughness (26, 27).

1.2.2 Evaluation of swallowing function

Protection of the airways is one of the primary functions of the larynx. The true vocal folds, false vocal folds and epiglottis act together as a sphincter to prevent food and foreign bodies entering the trachea (15). During the oropharyngeal phase of swallowing subglottic pressure builds up and elevation and anterior movement of the larynx occurs (15). Swallowing function can be evaluated by clinical swallowing examination, objective evaluation techniques, and by symptom specific HRQoL questionnaires (20, 28).

1.2.3 Patients perception of health-related quality of life

Patients self-evaluation of the health-related quality of life (HRQoL) provides insight in a patient's functioning and the severity of the perceived disability in social and/or professional life (18). HRQoL questionnaires can be disease specific and/or symptom specific. Cancer specific instruments have been developed to detect disease and treatment-related effects on HRQoL. Symptom specific instruments such as a voice or swallowing scale, which is frequently used for this research subject, have a smaller scope (20). To interpret the impact of the disease and treatment outcomes it is useful to evaluate HRQoL pre- and post-treatment.

1.3 Functional outcome in early laryngeal cancer

Over the past decades, numerous studies have evaluated the impact of early laryngeal cancer and its treatment outcomes (1, 3, 7, 10, 11, 13, 29-55). In evaluating and reporting this literature, several factors have to be kept in mind, namely: scope of the study, heterogeneity in patient groups, type of treatment, moment of follow-up, and diversity in assessment tools.

1.3.1 Pre-treatment voice characteristics and vocal functioning

The presence of a laryngeal tumor can lead to hoarseness and breathiness as well as change of voice pitch and intensity (7). Pre-treatment voices are characterized by higher frequency, lower intensity, and deviant values for perturbation measures and HNR (29, 50). Pre-treatment values for perturbation measures and HNR significantly deteriorate in direct proportion to the severity of the endoscopic cancer status (33). Patients and their partners assess their vocal performance before cancer treatment as significantly deteriorated (51). Tumors located at the glottis, especially with involvement of the anterior commissure, have a more deteriorating influence on voice quality compared to supra- and subglottic lesions (30, 37, 48). Other factors that might influence voice quality during pre-treatment evaluation are age and size of the diagnostic biopsy performed to determine whether the tumor is malignant (43). Overall, in early laryngeal cancer voice problems already exist before treatment due to the tumor itself, but there is limited literature describing the pre-treatment voice characteristics and functioning.

1.3.2 Voice characteristics and vocal functioning after laser surgery

Laser surgery can cause scarring and loss of tissue of the vocal folds which may affect vibration and can lead to a glottal gap (13). These side effects of this surgical treatment affect normal vocal fold closure, normal glottic vibrations, and resonance characteristics (7). In self-evaluation studies, patients undergoing laser surgery reported improvement (3, 41) as well as deterioration (53) in vocal performance. Sjögren and colleagues (44) perceptually assessed 37 patients with a follow-up time of six to 83 months post-treatment. In 59% of the cases breathiness is found and therefore this phenomenon is seen as a typical characteristic for the laser surgery treated voice(44). Meta-analysis of this subject report significant improvements in jitter and shimmer values in laser surgery treated patients more than 12 months after treatment (10, 35, 54). Van Gogh et al. (11) conducted a study (*n*=106) evaluating male voices of 67 laser surgery treated patients and 39 RT treated patients. Assessment took place pre-treatment and 3, 6, 12 and 24 months post-treatment. A quicker recovery of voice quality was reported in patients treated with laser surgery: 3 months post-treatment differences with normal voices are no longer detectable, except for fundamental frequency. Laser surgery treated voices remain higher pitched even at a follow-up time of 24 months (11).

1.3.3 Voice characteristics and vocal functioning after radiotherapy

Acute dysphonia after RT can be caused by edema (7). After 12 months follow-up, dryness and fibrosis can be a result of RT leading to reduced vocal fold vibration and laryngeal mobility (7, 13, 54, 55). Positive assessments in self-reported voice performance and acoustics are found (29, 36, 38, 40, 51). Significant improvement in voice parameters is demonstrated for intensity, frequency, perturbation parameters, HNR, and maximum phonation time (MPT). Intensity and MPT increased while frequency and perturbation parameters decreased after treatment (29, 36). In the study of Agarwal et al. (29) this improvement is seen three to six months post-treatment. Krengli et al. (36) assessed vocal functioning on the long-term and found similar results 24-120 months post-RT. These positive findings conflict with findings of a deviance in F_0, pitch range and jitter values when comparing RT treated patients with laser surgery treated patients or a control group (11, 35, 52). Verdonck-De Leeuw et al. (51) investigated the late effects of RT and reported a significant improvement in self-assessed vocal performance seven to ten years post treatment compared to the first years after treatment.

1.3.4 Pre- and post-treatment swallowing function

Evaluating swallowing function in early laryngeal cancer is a relative unexplored topic. Only two systematic reviews are found aiming at detecting swallowing difficulties in this patient group (13, 46). In Van Loon's review it is implicated that swallowing ability may be affected after RT because of dry mucosa, sticky mucus, and fibrosis (13). Two small cohort studies report swallowing outcomes (42, 47). Stoeckli et al. (47) described a negative impact of RT treated laryngeal malignancies on the ability to swallow solid food, investigated by self-evaluation assessment. Roh et al. (42) studied swallowing functioning by self-evaluation and videofluoroscopic swallowing study. A small group (*n*=19) of patients with laser surgery treated supraglottic carcinoma is assessed two weeks and one, three, six and twelve months after surgery. Although a deteriorated swallowing function is found shortly after treatment, in most cases this deterioration recovered within 3 to 6 months (42).

Overall, literature reports different results in voice and swallowing problems which leads to inconclusive evidence for expected outcomes after treatment.

2. Objectives, hypothesis and research question

2.1 Objectives

Over the last decades, improvements have been made in the treatment of early laryngeal cancer which lead to better survival rates. Secondary treatment outcomes such as voice characteristics, swallowing ability and HRQoL, are of growing importance in providing patient care.

As mentioned in chapter 1 (paragraph 1.3), literature on acoustic voice characteristics and self-reported voice problems yields various results. Comparing the findings of different studies is difficult, because of divergence in scope of these studies, diversity in assessment tools and heterogeneity in patient groups, types of treatment and moment of follow-up. Most of the existing studies are aimed at comparing the outcomes of two or more treatment groups, whilst alterations within the functioning of each patient separately might give new insights in the subject. Investigating acoustic outcomes in combination with patients' self-reported vocal performance provides knowledge regarding the daily clinical impact of voice problems and is therefore a valuable subject to investigate.

Another subject that deserves attention in early laryngeal cancer patients is the occurrence of swallowing problems before and after treatment. Anatomic and physiological alterations before and after cancer treatment are well known but there is limited knowledge about the presence and severity of possible swallowing problems due to these alterations. As discussed in chapter 1 (paragraph 1.3.4), only two studies are found investigating this subject which urges for more evidence.

It can be stated that conclusive evidence about the voice characteristics, vocal functioning and swallowing function of early laryngeal cancer patients is scarce. It is essential to gain more knowledge about this subject. Aim is to achieve the best oncological results with an optimal retention of function to maximize HRQoL in early laryngeal cancer patients.

2.2 Hypothesis

A research project is conducted to investigate voice quality and patients based experiences on vocal functioning and swallowing ability before and after treatment for early laryngeal cancer. It is hypothesized that, in patients with small laryngeal carcinomas, vocal or swallowing function is affected by cancer treatment, which may influence patients' HRQoL

2.3 Research questions

The following research question is formulated: *"What are acoustic characteristics of the voices of early stage laryngeal cancer patients and how do these patients rate their vocal performance and swallowing ability before and one year after cancer treatment?"* To answer the research question, several sub questions have to be addressed:

- What differences are detected in the acoustic analysis of voice recordings, the self-evaluation of vocal performance and self-evaluation of swallowing ability patients before and one year after cancer treatment?
    - Does tumor stage influence acoustic outcomes, self-reported vocal functioning and self-reported swallowing ability?
    - Does tumor site influence acoustic outcomes, self-reported vocal functioning and self-reported swallowing ability?
    - Does type of treatment influence acoustic outcomes, self-reported vocal functioning and self-reported swallowing ability?
- Is there a correlation between acoustic outcome values and self-reported health-related quality of life outcomes?

3. Method

3.1 Participants

Included in this study are patients with laryngeal cancer presented at the Netherlands Cancer Institute Antoni van Leeuwenhoek in the period between 2011 and 2013. Included are patients who have early laryngeal cancer stage T3 or less, are treated with laser surgery or RT and completed both a pre- as a post-treatment assessment.

3.2 Procedure

Before and ≥ 12 months after treatment patients were assessed at the Netherlands Cancer Institute by a clinical researcher or speech and language pathologist. Audio recordings were made of a read aloud text and a sustained vowel /a/. At this moment, HRQoL and symptom-specific QoL questionnaires were handed over to the patient with the instruction to return within a week.

3.3 Materials

Audio recordings were made with Audacity software. A headset with two microphones is used, one at 3 cm to mouth distance and one at 20cm to mouth distance. Calibration of the microphone is completed by Voice Profiler software. The Dutch text 'Tachtig dappere fietsers' is used.

Three symptom-specific quality of life questionnaires are used; The Voice Handicap Index (VHI) (19, 56), a linear analog scale assessment (LASA) and the EAT-10 (57). All questionnaires are translated into Dutch. The VHI is a widely used validated questionnaire for measuring voice problems in daily life (19, 56, 58). The VHI contains 30 questions grouped into three subscales: *physical*, *functional* and *emotional* (19, 56). In the LASA questionnaire, participants are asked to rate statements about *voice*, *communication* and *swallowing* on a severity scale from one to ten. The EAT-10 (57) is a validated ten item questionnaire which assesses dysphagia (57). Containing ten items that should be rated on a zero to four scale of severity, this questionnaire contains no subscales. For the questionnaires EAT-10, VHI and LASA swallowing a higher score indicates a higher impact on HRQoL. In the LASA voice and LASA communication questionnaires a lower score indicates a higher impact on HRQoL.

The computer software Praat (59) and IBM SPSS 22.0 (60) are used to analyze the obtained data.

3.4 Analysis

Acoustic analysis of the audio data is obtained with the software Praat (59). First, segmentation of the running speech file is performed. After segmentation the acoustic parameters of interest are obtained. The acoustic parameters and outcomes on HRQoL questionnaires are collected in a database and statistically analyzed using the software IBM SPSS 22.0 (60).

3.4.1 Acoustic analysis

In both audio files segmentation is carried out manually after visual inspection. Pre- and post-treatment assessments of each patient are analyzed one after the other in order to prevent inconsistency in the analysis. For the read aloud text, incorrect repetitions and outspoken comments are removed. One stable second of the sustained vowel /a/ is selected. Before analysis of the running speech file, the intensity is equalized to 60 dB. In analyzing the F_0 pitch floor is set to 20Hz and pitch ceiling to 400Hz. Before analyzing the HNR the minimum pitch is set to 20Hz.

Parameters of interest for the read aloud text are voicedness (%), and mean F_0 (Hz). Percentages of voiced frames are extracted to obtain information about changes in amount of voicedness in the text. F_0 values are analyzed to obtain information about alterations in pitch.

Parameters of interest for the sustained vowel /a/ are voicedness (%), mean F_0 (Hz), SD F_0 (Hz), HNR (dB), local jitter (%), and local shimmer (dB). Percentages of voiced frames in the vowel /a/ give information about the patients' ability to produce a voiced continuous vowel. Mean F_0 measurements provide information about pitch and alterations in pitch. With SD of the F_0 pitch fluctuations within the vowel are measured. In this research project alterations in F_0 are main subject of interest therefore F_0 values of males and females are analyzed together. With HNR and perturbation measurements information about regularity and noise components are obtained.

3.4.2 Statistical analysis

Statistical analysis is completed within the created SPSS database containing patients' characteristics, acoustic outcomes, and self-reported outcomes. For descriptive statistics median, standard deviation and visualizations of the data are required. Statistical testing is conducted by means of student's t-tests when equal variance can be assumed, Welch's t-test is used when equal variance is not assumed. Strengths of correlations are measured with Pearson's correlation coefficient. Correlations are tested among the created difference variables, which show the alteration within patients between pre- and post-treatment measurement. Correlating measurements provide information of the usability and equivalence of the used parameters. The level of statistical significance when testing a statistical hypotheses is held at alpha 0.05.

4. Results

Data from 20 patients who had completed both pre- and post-treatment assessment, is obtained and analyzed. Mean follow-up time is 16 months after treatment. Pre-treatment HRQoL questionnaires are completed by fifteen patients, and post-treatment by sixteen patients. Fifteen patients (75%) completed both pre- and post-treatment HRQoL. From all included patients voice characteristics are obtained. For the subgroups supraglottic and T3, no statistical analyses took place because these groups were too small to analyze (*n*=2 and *n*=2).

4.1 Patient characteristics

Patient characteristics are presented in table 1. The included group contains 18 male and two female patients. Mean age at pre-treatment date is 60 years, range 40 – 74 years. Malignant lesions are staged T1 (*n*=9) T2 (*n*=9) or T3 (*n*=2) and divided based on location at the glottis (*n*=18) or supraglottis (*n*=2). One patient was diagnosed with a transglottic tumor. This patient is included in the group of patients with a glottic tumor. Fourteen patients (70%) received radiotherapy, six patients (30%) were treated with laser surgery. Table 2, 3 and, 4 show division of the sub groups in crosstabs. In the group RT treated patients all included tumor stages are represented: T1 (*n*=5), T2 (*n*=7), and T3 (*n*=2); and both included tumor sites: glottic (*n*=12) and supraglottic (*n*=2). In the group of laser surgery treated patients only T1 (*n*=4) and T2 (*n*=2) tumors are seen and all tumors are located at the glottis.

Table 1. Characteristics of the 20 included patients

N = 20		count	%	mean
sex	female	2	10 %	
	male	18	90 %	
age; ranged 40 – 74				60
T-classification	T1	9	45 %	
	T2	9	45 %	
	T3	2	10 %	
tumor site	supraglottis	2	10 %	
	glottis	18	90 %	
type of treatment	laser surgery	6	30 %	
	RT	14	70 %	

Table 2. Crosstab denote patients' (*n*) tumor location and received type of treatment.

		tumor site		
		supraglottis	glottis	total
type of treatment	laser	0	6	6
	RT	2	12	14
total		2	18	20

Table 3. Crosstab denote patients' (*n*) t-classification and received type of treatment.

		t-classification			
		T1	T2	T3	total
type of treatment	laser	4	2	0	6
	RT	5	7	2	14
total		9	9	2	

Table 4. Crosstab denote patients' (*n*) tumor location and t-classification.

		tumor site		
		supraglottis	glottis	total
t-class	T1	0	9	9
	T2	2	7	9
	T3	0	2	2
total		2	18	20

4.2 Baseline characteristics

4.2.1 Pre-treatment voice characteristics

Values for the pre-treatment voice parameters are presented in table 5. No significant differences were found using Welch's t-test in comparing pre-treatment values for tumor stage.

Table 5. Pre-treatment voice parameters for site and stage.

	overall n=20	*glottic n*=18	*supraglottic n*=2	*T1 n*=9	*T2 n*=9	*T3 n*=2
voicedness text (%)	59 ± 10	59 ± 10	65 ± 8	62 ± 8	59 ± 13	60 ± 1
mean F0 text (Hz)	142 ± 27	142 ± 25	162 ± 55	156 ± 24	142 ± 29	133 ± 38
voicedness /a/ (%)	100 ± 3	100 ± 3	100 ± 0	100 ± 1	100 ± 4	100 ± 0
mean F0 /a/ (Hz)	123 ± 42	123 ± 43	143 ± 42	131 ± 44	113 ± 44	147 ± 37
SD F0 /a/ (Hz)	1 ± 19	2 ± 20	1 ± 0	2 ± 20	1 ± 21	1 ± 0
HNR /a/	15 ± 6	14 ± 6	18 ± 2	14 ± 5	16 ± 7	14 ± 1
jitter /a/ (%)	0.51 ± 1.52	0.57 ± 1.58	0.42 ± 0.03	0.60 ± 1.14	0.49 ± 1.98	0.48 ± 21.00
shimmer /a/ (dB)	5.77 ± 6.19	6.75 ± 6.37	3.29 ± 0.50	7.01 ± 5.11	3.64 ± 7.79	4.62 ± 2.63

Figure denote median ± SD.

4.2.2 Pre-treatment self-perception of health-related quality of life

In table 6 values for the pre-treatment HRQoL outcomes are presented. Comparison of means of tumor staging groups are tested with independent t tests. In patients with a T1 tumor a significant higher impact on total VHI is seen compared to patients with a T2 tumor ($t(10) = 3.32$, $p = .008$). This difference in outcome is also seen comparing these two tumor stage groups based on the physical VHI sub-score ($t(8) = 2.40$, $p = .008$).

Table 6. Pre-treatment HRQoL parameters for site and stage. *n*=20.

	overall n=15	*glottic n*=13	*supraglottic n*=2	*T1 n*=5	*T2 n*=8	*T3 n*=2
VHI functional	12 ± 6	13 ± 6	6 ± 1	12 ± 7	8 ± 5	17 ± 2
VHI physical	17 ± 5	18 ± 5	13 ± 4	22 ± 5*	15 ± 3*	21 ± 4
VHI emotional	4 ± 7	7 ± 7	2 ± 1	12 ± 8	2 ± 5	7 ± 4
total VHI	35 ± 16	40 ± 15	20 ± 5	47 ± 16*	23 ± 12*	44 ± 10
EAT-10	0 ± 2	0 ± 3	1 ± 0	0 ± 4	0 ± 0	0 ± 0
LASA voice	20 ± 4	20 ± 4	22 ± 6	20 ± 2	22 ± 4	16 ± 4
LASA communication	16 ± 5	16 ± 5	21 ± 9	16 ± 2	17 ± 7	15 ± 10
LASA swallowing	2 ± 7	0 ± 8	6 ± 2	0 ± 4	3 ± 9	2 ± 2

Figure denote median ± SD. Independent t test 2-tailed significance level: *$p \leq .05$

4.3 Comparison between baseline and one-year follow-up

In the following sections difference variables are presented. Difference variables are created by subtracting pre-treatment values from the post-treatment outcome values.

Table 7. Overall difference between pre- and post-treatment voice characteristics

	Overall n=20
voicedness text (%)	-3.50 ± 10.64
Mean F0 text (Hz)	-12.00 ± 25.78
voicedness /a/ (%)	0.00 ± 16.32
Mean F0 /a/ (Hz)	-3.50 ± 51.26
SD F0 /a/ (Hz)	0.00 ± 15.20
HNR /a/	0.00 ± 8.69
jitter /a/ (%)	-0.11 ± 1.41
shimmer /a/ (dB)	-1.45 ± 6.73

Figure denote post-treatment minus pre-treatment values, median ± SD.

4.3.1. Alterations in voice characteristics

Calculated variables representing the difference between post- and pre-treatment for voice parameters are presented in table 7 and table 8. Table 7 shows the overall changes in voice parameters for all participants. In table 8 parameters are presented divided by site, stage and type of treatment. Voicedness of the text decreases in most patients compared with pre-treatment levels. When analyzing voicedness of the sustained vowel /a/, median values post-treatment are comparable with pre-treatment level. High SD values for voicedness of the /a/ are seen in the group of glottic tumors, group of T2 tumors and the RT treated group. In the read aloud text a decrease of mean F_0 is noticed. In the laser surgery treated group, an increase in F_0 of the sustained vowel is found, compared with a decrease of F_0 in the RT treated group, plotted in figure 1. HNR increases post-treatment in the group of patients with T2-staged tumors and in the laser surgery group. Perturbation measurements decrease post-treatment. No significance is found for these findings using Welch's t-test.

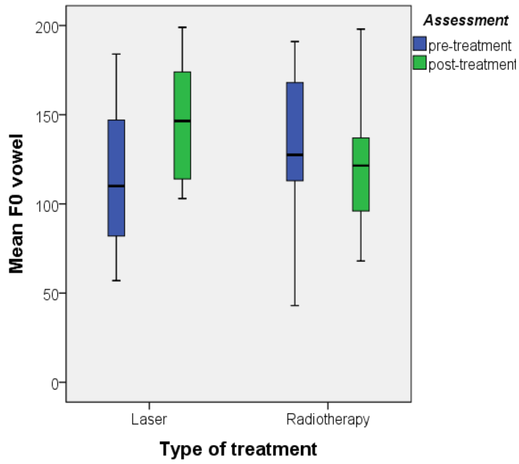

Figure 1. Alterations in mean F_0 of the vowel /a/ for type of treatment

Table 8. Difference variables voice parameters for site, stage and treatment modality.

	Glottic n=18	*Supraglottic n*=2	*T1 n*=9	*T2 n*=9	*T3 n*=2	*Laser n*=6	*RT n*=14
voicedness text (%)	-4.50 ± 11.09	0.50 ± 3.54	-5.00 ± 10.20	-2.00 ± 11.25	1.50 ± 2.12	-5.00 ± 10.00	-3.00 ± 11.02
Mean F0 text (Hz)	-15.00 ± 25.23	-4.50 ± 20.51	-15.00 ± 24.08	-15.00 ± 26.06	-25.00 ± 31.11	-12.00 ± 18.83	-19.00 ± 27.72
voicedness /a/ (%)	0.00 ± 17.22	0.00 ± 0.00	0.00 ± 0.71	0.00 ± 24.61	0.00 ± 0.0	0.00 ± 4.80	0.00 ± 19.08
Mean F0 /a/ (Hz)	-9.50 ± 54.06	12.50 ± 16.26	0.00 ± 55.40	1.00 ± 43.59	-62.5 ± 13.44	18.00 ± 58.29	-13.00 ± 45.24
SD F0 /a/ (Hz)	0.00 ± 19.66	-0.50 ± 0.71	0.00 ± 20.34	-1.00 ± 19.90	0.00 ± -1.00	-0.50 ± 10.21	0.00 ± 21.75
HNR /a/	-1.00 ± 9.10	4.00 ± 4.24	-1.00 ± 10.19	3.00 ± 7.37	-5.50 ± 4.95	4.00 ± 11.86	0.00 ± 7.21
jitter /a/ (%)	-0.04 ± 1.48	-0.16 ± 0.10	-0.01 ± 1.25	-0.17 ± 1.71	0.38 ± 0.06	-0.34 ± 1.15	-0.11 ± 1.51
shimmer /a/ (dB)	-2.20 ± 7.04	-0.49 ± 2.03	-3.42 ± 7.17	-1.92 ± 6.93	2.10 ± 2.01	-4.51 ± 8.00	-0.65 ± 6.44

Figure denote post-treatment minus pre-treatment values, median ± SD.

4.3.2 Correlations of acoustic parameters

Table 9 presents correlations between the acoustic parameters of interest. A significant positive correlation is seen between mean F_0 for the vowel /a/ and mean F_0 in the read aloud text ($r(18) = .486$, $p = .041$). Indicating that when F_0 decreases in the vowel, it will also decrease in the read aloud text. When percentage of voicedness of the vowel decreases a decrease in SD of F_0 of the vowel /a/ is seen ($r(18) = .579$, $p = .012$). As shown in figure 2 this effect is caused by one patient who had a decrease in SD F_0 and decrease in voicedness. Significant is the positive correlation in mean F_0 and HNR of the vowel /a/ ($r(18) = .770$, $p = <.000$). Indicating that voices of patients who have an increased F_0 increase in harmonic components, figure 3. Strong statistically significant correlations are revealed between the perturbation measurements and the SD of the F_0 of the sustained vowel: jitter and SD F_0 ($r(18) = .862$, $p = <.000$) as well as shimmer and SD F_0 ($r(18) = .695$, $p = .001$). HNR of the vowel /a/ shows a strong negative correlation with jitter ($r(18) = -.576$, $p = .008$) and shimmer ($r(18) = -.782$, $p < .001$). Jitter and shimmer measurements of the sustained vowel are strongly correlated ($r(18) = .837$, $p < .001$).

Table 9. Correlations between difference variables of acoustic parameters and self-perception of HRQoL parameters.

	% voiced text	Mean F0 text	% voiced /a/	mean f0 /a/	SD f0 /a/	HNR /a/	% jitt /a/
Mean F0 text	.391	-	-	-	-	-	-
% voiced /a/	.283	.256	-	-	-	-	-
mean f0 /a/	.405	.486*	.360	-	-	-	-
SD f0 /a/	-.197	-.246	.579*	-.265	-	-	-
HNR /a/	.322	.420	.250	.770*	-.342	-	-
% jitt /a/	-.024	-.314	.272	-.328	.862*	-.576*	-
shimm dB /a/	-.234	-.332	.177	-.401	.695*	-.760*	.837*

Figure denote *R.* Significance level: *$p \leq .05$

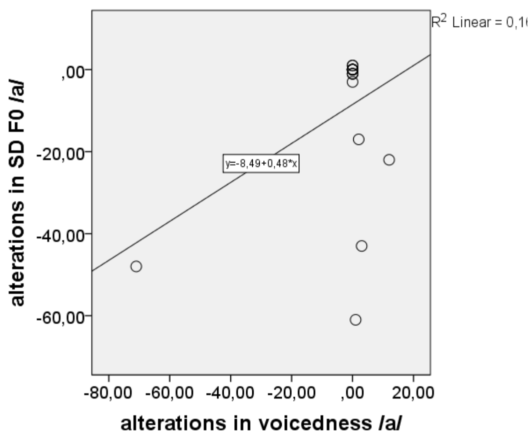

Figure 2. Scatterplot showing SD F_0 /a/ and voicedness /a/.

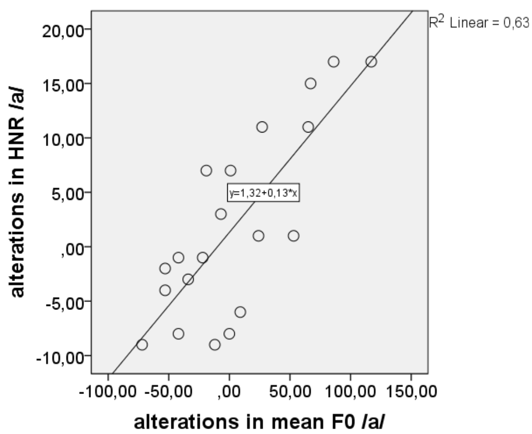

Figure 3. Scatterplot showing mean F_0 /a/ and HNR /a/.

4.3.3 Alterations in self-perception of health-related quality of life

In table 10 and 11 variables are presented representing the difference between post- and pre-treatment for the self-reported HRQoL. Table 10 shows the overall changes in HRQoL for all patients. In table 11 parameters are presented divided by site, stage and type of treatment.

Independent t tests showed a significant difference in total VHI outcome based on tumor stage: patients with T1 tumors reported a larger decrease in voice handicap (meaning improvement in HRQoL) compared to patients with T2 tumors ($t(7)= -3.60$, $p = .009$). This effect for tumor stage is shown in figure 4. A similar significant effect is seen in the sub scores measuring voice related QoL, namely: VHI functional ($t(7)= -3.04$, $p = .019$), VHI physical ($t(9)= -4.56$, $p = .001$), LASA voice (t=(7)3.70, p=.008) and LASA communication ($t(7)= 3.30$, $p = .013$). No significance is found for type of treatment, even though laser surgery treated patients show an evident decrease in voice handicap as shown in figure 5.

Table 10. Overall difference between pre- and post-treatment HRQoL

	Overall n=15
VHI functional	-4.00 ± 6.44
VHI physical	0.00 ± 7.22
VHI emotional	-4.00 ± 8.45
Total VHI	-6.00 ± 20.73
EAT-10	2.00 ± 4.27
LASA Voice	7.00 ± 7.37
LASA comm	3.00 ± 5.87
LASA swal	0.00 ± 7.37

Figure denote post-treatment minus pre-treatment values, median ± SD.

Table 11. Difference variables self-perception of HRQoL parameters for site, stage and treatment modality.

	Glottic n=13	*Supraglottic n*=2	*T1 n*=5	*T2 n*=8	*T3 n*=2	*Laser n*=4	*RT n*=11
VHI functional	-5.00 ± 6.83	-1.00 ± 4.24	-10.00 ± 5.00*	0.00 ± 4.21*	1.50 ± 0.71	-4.00 ± 9.90	-4.00 ± 6.29
VHI physical	-4.00 ± 8.44	-0.50 ± 7.78	-16.50 ± 5.06*	-4.00 ± 5.15*	-1.00 ± 2.83	-4.00 ± 7.51	-5.00 ± 8.91
VHI emotional	-2.00 ± 7.41	4.00 ± 0.00	-9.00 ± 4.55	2.00 ± 5.83	6.00 ± 5.66	-2.50 ± 6.36	0.00 ± 7.75
Total VHI	-22.00 ± 20.98	2.50 ± 12.02	-36.00 ± 11.73*	-1.00 ± 13.66*	6.50 ± 3.54	-14.00 ± 21.21	-6.00 ± 21.93
EAT-10	0.00 ± 3.99	5.50 ± 4.95	0.00 ± 3.00	2.00 ± 4.28	3.00 ± 1.41	1.00 ± 1.41	2.00 ± 4.71
LASA Voice	7.00 ± 7.89	9.50 ± 6.36	19.00 ± 2.89*	4.00 ± 5.19*	3.00 ± 5.66	8.00 ± 9.07	6.00 ± 7.29
LASA comm	3.00 ± 5.43	3.00 ± 9.90	10.50 ± 1.41*	2.00 ± 5.24*	1.00 ± 2.83	6.00 ± 5.66	3.00 ± 6.23
LASA swal	0.00 ± 7.70	4.50 ± 3.54	0.00 ± 3.00	0.00 ± 8.89	8.00 ± 4.24	0.00 ± 0.58	0.00 ± 8.63

Figure denote post-treatment minus pre-treatment values, median ± SD.
Independent t test 2-tailed significance level: *$p \leq .05$

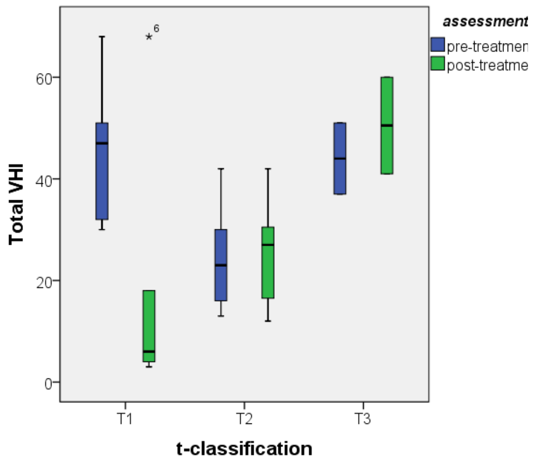

Figure 4. Alterations in total VHI for t-classification.

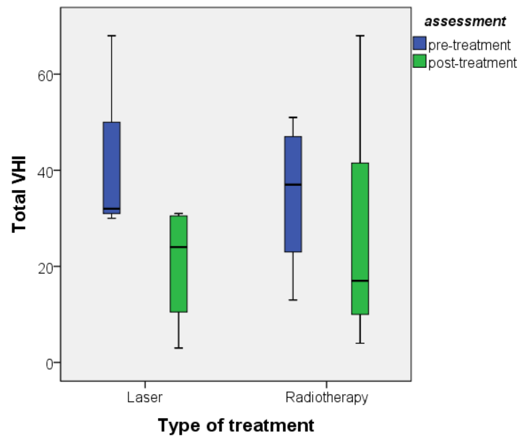

Figure 5. Alterations in total VHI for type of treatment.

4.3.4 Correlation of health-related quality of life parameters

Correlation between self-perception of HRQoL questionnaires are presented in table 12. Total VHI score and all its sub scores are strongly positive correlated, namely; Total VHI and VHI functional ($r(11) = .943$, $p < .001$), total VHI and VHI physical ($r(11) = .931$, $p < .001$), total VHI and VHI emotional ($r(11) = .931$, $p < .001$), VHI physical and VHI functional ($r(11) = .811$, $p = .002$). VHI emotional and VHI functional ($r(11) = .001$, $p = .856$), and VHI emotional and VHI physical ($r(11) = .769$, $p = .006$). Scores on the functional outcome of the VHI show a significant negative correlation with LASA communication ($r(10) = -.730$, $p = .017$). For the physical sub score of the VHI a significant positive correlation is revealed with the EAT-10 outcomes ($r(11) = .841$, $p < .001$). Outcomes on the physical sub score of the VHI are negatively correlated with LASA voice ($r(11) = -.737$, $p = .010$) and communication ($r(11) = .840$, $p < .001$). Outcomes on the EAT-10 show a positive correlation with the emotional sub score of the VHI ($r(10) = .652$, $p = .041$) and with the total score of the VHI ($r(10) = .789$, $p = .007$). Total VHI outcome is negative correlated with LASA communication ($r(10) = -.747$, $p = .013$) and positive correlated with LASA swallowing outcomes ($r(10) = .739$, $p=.015$). Scores on the LASA communication and EAT-10 show a negative correlation ($r(11) = -.762$, $p = .006$). A strong positive correlation is seen between LASA voice and LASA communication ($r(10) = .830$, $p = .003$).

Table 12. Correlations between difference variables of acoustic parameters and self-perception of HRQoL parameters.

	VHI F	VHI P	VHI E	Total VHI	EAT-10	LASA voice	LASA comm
VHI P	.811*	-	-	-	-	-	-
VHI E	.856*	.769*	-	-	-	-	-
Total VHI	.943*	.931*	931*	-	-	-	-
EAT-10	.606	.841*	.652*	.789*	-	-	-
LASA voice	-.614	-.737*	-.314	-.591	-.617	-	-
LASA comm	-.730*	-.840*	-.499	-.747*	-.762*	.830*	-
LASA swal	.560	.328	.640	.739*	-.042	-.147	-.092

Figure denote *R.* Significance level: *$p \leq .05$

4.3.5 Correlations of acoustic and health-related quality of life parameters

Table 13 presents correlations between acoustic parameters and outcomes on self-perception of HRQoL. A strong significant positive correlation is detected between percentage of voicedness in the text and outcomes on the VHI functional ($r(11) = .771$, $p = .005$.). Percentage of voicedness of the text also correlates positive with the total outcome on the VHI ($r(11) = .603$, $p = .050$). Indicating that patients with higher values for voicedness experience more voice handicap, figure 6 shows the contribution of this effect. One patient who experienced improvement in voice handicap decreased in voicedness of the text. A significant positive correlation is seen in mean F_0 in the text and EAT-10 outcome ($r(11) = .728$, $p = .017$). The higher the impact on swallowing problems the higher the F_0, shown in figure 7. In lower scores on self-perceived swallowing problems, measured with LASA swallowing, lower mean F_0 values for the vowel /a/ are seen ($r(12) = -.626$, $p = .039$). Increase in SD F_0 of the /a/ leads to increased reported swallowing problems on the LASA swallowing ($r(12) = .770$, $p = .006$). Similarly high jitter values of the /a/ are correlated to high LASA swallowing scores ($r(12) = .608$, $p = .036$).

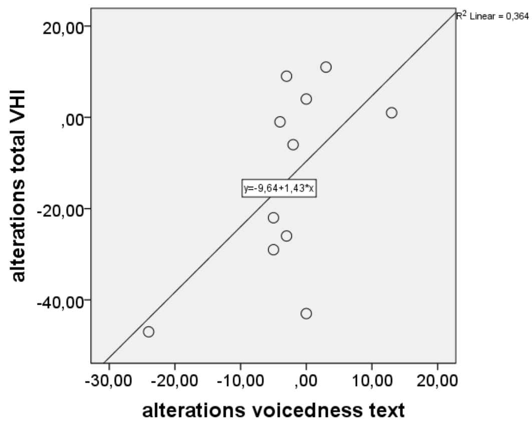

Figure 6. Scatterplot showing total VHI and voicedness text.

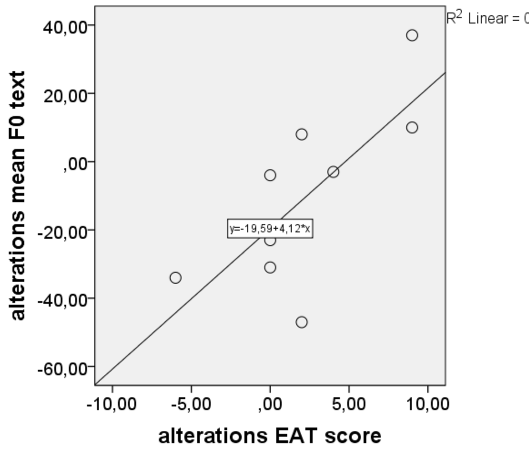

Figure 7. Scatterplot showing mean F_0 text and EAT score.

Table 13. Correlations between difference variables of acoustic parameters and self-perception of HRQoL parameters.

	VHI functional	VHI physical	VHI emotional	Total VHI	EAT-10	LASA voice	LASA comm	LASA swal
% voiced text	.771*	.207	.490	.603*	.440	-.016	-.602	-.299
Mean F0 text	.485	.371	.155	.404	.728*	-.417	-.528	-.413
% voiced /a/	.311	.075	.137	.189	.123	-.061	-.233	-.240
Mean f0 /a/	-.47	-.117	-.319	-.220	.098	.094	-.179	-.626*
SD f0 /a/	-.409	-.077	-.177	-.224	-.501	.204	.350	.770*
HNR /a/	-.106	-.210	-.239	-.200	.151	-.111	-.055	-.391
% jitt /a/	.554	.292	.436	.470	-.334	.055	.069	.608*
shimm dB /a/	.279	.322	.291	.323	-.208	.051	-.001	.549

Figure denote *R*. Significance level: *$p \leq .05$

5. Discussion

5.1 Discussion of the results

5.1.1 Voice characteristics, vocal performance, and swallowing ability outcomes in perspective

In chapter 2 the following research question was addressed: 'What differences are detected within speakers before and one year after laryngeal cancer treatment in the acoustic analysis of voice recordings, the self-evaluation of vocal performance and self-evaluation of swallow ability?' In this section the general results will be interpreted and compared with the evaluated literature.

To begin with, the first sub question that is addressed will be discussed; 'Does tumor stage influence acoustic outcomes, self-reported vocal functioning and self-reported swallowing ability?' For this question, statistically comparison was only possible between the group of patients with T1 and the group of patients with T2 staged tumors. At baseline no significant differences between the two stages are found in the acoustic parameters. When evaluating the HRQoL outcomes patients with a T2 staged tumor report better vocal functioning before oncological treatment. This is demonstrated for the total VHI score and its physical sub score when comparing patients with T2 staged tumors to patients with T1 tumors (shown in table 11 and figure 4, paragraph 3.3.4). This finding, however, is not in line with the findings of Galetti et al. (33) which conclude that pre-treatment voice problems increase in direct proportion to the severity of the endoscopic status. In several studies it is explicated that involvement of the anterior commissure has a more deteriorating effect on vocal performance (30, 37, 48). However in this study exact location and extension of the tumors is not investigated, It is plausible that in this study the T1 staged tumors are more often located at the anterior commissure. Noteworthy in this context is that in this research group all supraglottic tumors are T2 staged. This could lead to a bias when concluding that before treatment patients with T2 staged tumors rate their vocal functioning better compared to patients with T1 staged tumors. When comparing baseline and post-treatment HRQoL more favorable outcomes are seen in the voice related HRQoL questionnaires for patients with T1 tumors after oncological management. This could be explained by the fact that the patients with T1 staged tumors experience more voice problems pre-treatment and make a greater improvement in voice functioning compared to the T2 staged group after treatment. In none of the evaluated studies in chapter 1 a similar tendency is found.

The second sub question that is addressed was: 'Does tumor site influence acoustic outcomes, self-reported vocal functioning and self-reported swallowing ability?' In this study group no inferential statistics could be performed on the sub groups for tumor site because of the group of patients with supraglottic tumors was too small (*n*=2). In evaluating the tendencies a decrease in VHI score is seen after treatment in patients with glottic tumors, in contrast to a slight increase for patients with supraglottic tumors (figure 8). This effect could be explained by the fact that glottic tumors induce voice problems as an effect of the tumor. Removal of the tumor therefore leads to better vocal functioning. Voice problems after treatment for a supraglottic tumor can occur as a result of secondary treatment effects. No comparable outcomes are found in the evaluated literature.

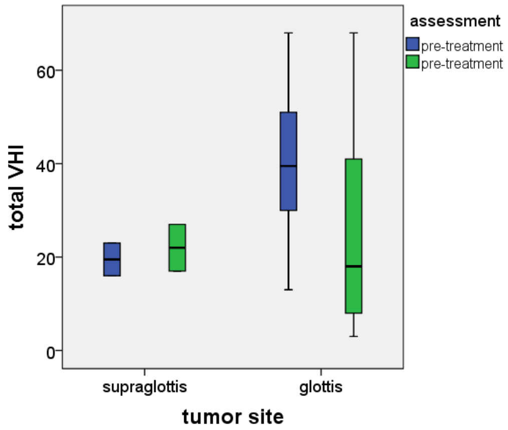

Figure 8. Alterations in total VHI for tumor site.

And finally the third sub question that is addressed; 'Does type of treatment influence acoustic outcomes, self-reported vocal functioning and self-reported swallowing ability?' For the acoustic comparison pitch alterations are notable. In the sustained vowel, F_0 values decrease after RT whilst an increase is seen after laser surgery (figure 1). This finding is comparable with the findings of Van Gogh et al. (11) who concluded that after laser surgery no significant alterations are detectable, except for F_0 which remains higher pitched. Lower values for F_0 after RT could be an effect of oedema. Higher post-treatment values for F_0 for the laser surgery group can be an effect of insufficient mobility of the vocal folds and compensatory hyperkinetic voicing. Scores on the EAT and LASA swallowing did not show significant differences for type of treatment. Wide SD for self-reported swallowing problems are seen which supports the estimation that swallowing ability is affected in some patients after treatment. Both treatment options show a decrease in VHI after treatment (figure 5). After laser surgery only improvement is seen in vocal functioning whereas after RT also deterioration of vocal functioning is seen. No significance is found for the self-reported HRQoL parameters. In the evaluated literature deteriorating short term effects of RT and laser surgery are found and improvement on the long term (12 to 24 months) post-treatment (11, 29, 36, 50). The data of this research group could be indicated as long term post-treatment data with a mean follow-up of sixteen months. Outcomes do not confirm nor deny the evidence that one year post-treatment outcomes for both treatment modalities are comparable since significance is not revealed.

5.1.2 Correlations of outcome measurements in perspective

Responding to the last sub question addressed; 'Is there any correlation between acoustic outcome values and self-reported health-related quality of life outcomes?'

When investigating the interpersonal changes in acoustics before and after treatment several findings are notable. Perturbation measurements show the strongest correlations in the acoustic alterations. Increase in SD of the F_0 of the vowel leads to increased jitter and shimmer values. HNR is negatively correlated with perturbation measurements. Indicating that voices with high jitter and shimmer values contain a lower harmonic component and a higher additive noise component. This is consistent with the expected, whilst all measurement are F_0 dependent. High perturbation measurements are an indicator for breathy or hoarse voices. Therefore it is likely that these voices contain more noise and less harmonic components. Alteration in F_0 of the sustained vowel correlates slight positive with F_0 values of the read aloud text. This confirms that both parameters express a comparable aspect, which provides information about the usability of the parameters. In most current research acoustic analysis is only obtained in sustained vowels, whereas some investigators recommend evaluating pathological voice quality in running speech (21, 43). An advancement of analyzing as well running speech as a sustained vowel is the fact that it provides comparable but also complementary information; running speech offers a more natural setting of phonation.

In evaluating correlations of self-perceived HRQoL several associations are seen. Strongest correlations are revealed for the total score and sub scores of the VHI. An increase in the functional score of the VHI leads to a an increase in total score of the VHI. This is in line with the expected. Scores on the functional outcome of the VHI show a negative correlation with LASA communication. If a high impact on VHI and its functional sub score is revealed a high impact is expected on the LASA communication. The positive correlation between LASA voice and LASA communication indicate a related dimension. The correlations of the three scales VHI, LASA communication and LASA voice conforms the potential validity of LASA as a suitable instrument to assess the presence and degree of self-perceived vocal dysfunction. EAT-10 score is related to outcomes on the VHI and LASA communication, indicating that patients' experience of voice problems is related to swallowing problems or that patients that experience voice problems are more likely to experience swallowing problems. A non-significant effect is revealed in the correlation of LASA swallowing and EAT-10 score. Indicating that both questionnaires measure different aspects.

When evaluating the correlation of acoustic variables with self-reported parameters debatable outcomes are found. The positive correlation between percentages of voicedness of the text and VHI outcomes is notable, shown in figure 6 and figure 9. A negative correlation is what was expected. High values on the VHI indicate a severe impact whereas high values on voicedness in the text indicate sufficient phonation. Therefore, a more logical consequence would be that a decrease in voicedness would coexist with increased scores on the VHI (indicating higher impact). The strong correlating effect in this case is caused mainly by one patient (figure 6 and figure 9). When this potential outlier would be excluded outcomes could be less correlating. A positive correlation between EAT-10 score and mean F_0 of the text is seen (figure 7). This points to the statement that patients with a higher fundamental frequency more likely experience swallowing problems. This could be an effect of the more effort patients need to put in swallowing and phonation which leads to a higher pitch. However, an inversed effect is seen in the negative correlation between LASA swallowing outcomes and mean F_0 of the sustained vowel, where an increase in fundamental frequency results in less impact on swallowing problems. Both correlations between pitch and self-reported swallowing problems are discussable. As described EAT-10 and the LASA swallowing are not related, it could be that another aspect is induced. Jitter values and SD of the F_0 of the vowel /a/ correlate positively with impact on the LASA swallowing. This could be indicating that reduced voice quality and self-perceived swallowing problems are associated.

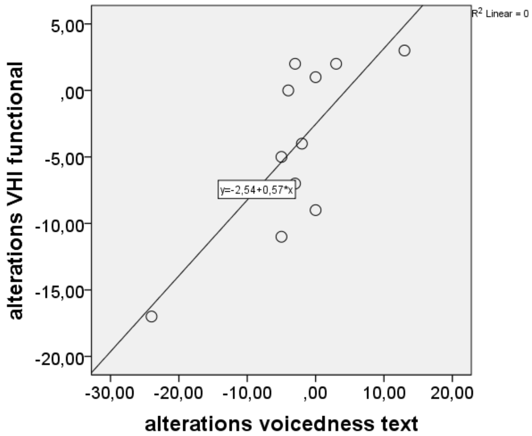

Figure 9. Scatterplot showing VHI F and voicedness text.

5.2 Limitations and strengths of the study

This study had some limitations. The nonrandomized design and small sample size result in limited (statistical) power. No inferential statistics could be performed for the group of patients with T3 staged tumors and the group of patients with supraglottic tumors (*n*=2, *n*=2, resp.). Heterogeneity of the group leads to complexity in interpretation of the results. When significant outcomes are revealed, underlying subgroups should always be taken into account. In comparing type of treatment it must be noticed that the comparability of the separate tumor groups is doubtful. The group of laser surgery treated patients contains only T1 and T2 staged tumors, the group of RT treated patients contains T1, T2 and T3 tumors. Smaller lesions are mostly selected for laser surgery whilst more extended lesions and supraglottic lesions are mostly selected for RT, leading to treatment bias. In this study, type and extent of laser excision was not well documented for all cases and therefore not included as a group marker. This is a shortcoming since earlier studies concluded that precise notification of extent of the laser excision and involvement of the anterior commissure are important grouping variables (30, 46). Baseline values of this group of patients were not compared with voice characteristics and HRQoL of healthy speakers. Only total scores and sub scores of the HRQoL questionnaires are analyzed and evaluated. More and precise information would be obtained when the questions would be analyzed separately. This would lead to more specific information about i.e. saliva problems or effortful speaking. Especially for the LASA, analyzing the questions separately would be more relevant, each question measures a different aspect.

Strength of the present study is the division in subgroups created for tumor stage and extension. Earlier studies mostly aimed at treatment differences and did evaluate mostly heterogeneous groups of tumor site and extension. Although in this study the included sub groups for T3 staged tumors and supraglottic tumors were relative small, the outcomes do provide insights for further research. The combination of evaluating objective acoustic information with subjective self-reported HRQoL aspects is another advancement of this study, especially because this study contains pre-treatment as well as one year post-treatment assessment. In most studies only post-treatment effects are evaluated. Another onward aspect of this study is the evaluation of acoustic voice quality in as well sustained vowels as running speech. This provides information about functional voicing.

6. Conclusion

6.1 Synopsis of key findings

This thesis describes a prospective study providing insight in acoustics and HRQoL of early laryngeal cancer patients from baseline to one year after treatment. To answer the two main research questions:

What differences are detected within speakers before and one year after cancer treatment in the acoustic analysis of voice recordings, the self-evaluation of vocal performance and self-evaluation of swallowing ability?

Before treatment a significant impact on self-reported voice functioning is found for patients with T1 staged tumors compared to patients with T2 staged tumors ($t(10) = 3.32$, $p = .008$). Patients with T1 staged tumors show an improvement in vocal functioning after treatment compared to patients with T2 staged tumors where deterioration in vocal functioning is seen (VHI; $t(7)= -3.60$, $p = .009$). No significance is found in evaluating self-perceived swallowing problems for the sub-groups. Deviating scores are seen as well pre- as post-treatment with respect to a an expected 0-score in case no swallowing problems exist. Presence of (slight) swallowing problems can be concluded, though not specified for any sub-group. Tendencies are seen in the acoustic analyzes for t-classification and type of treatment. Fundamental frequency of voices of patients treated with laser surgery increases one year post-treatment compared to a decrease that is seen for RT treated patients. A wide range for SD values is seen in perturbation measurements, F_0 values and measurements of voicedness, indicating the existence of voice problems and diversity of vocal functioning in this patient group.

Is there any correlation between acoustic outcome values and self-reported health-related quality of life outcomes?

Parameters of interest showed several significant correlations within their scope of measurement. Several acoustic outcome measurements correlated with each other. Perturbation measurements were strongly correlated, as consistent with the expected. F_0 values retrieved out of a continuous vowel and running speech were correlated. HRQoL measuring vocal functioning were strongly This correlations are expected and support the evidence for the usability of these outcome measurements. Correlations of the LASA questionnaire did not correlate well with the validated VHI and EAT-10. Summarizing this questionnaire in categories lead to less useable outcome measures. Evaluating the outcomes and correlations of the separate questions would presumably lead to more evident outcomes. When evaluating the correlations between acoustics parameters and HRQoL outcomes weak correlations and debatable correlations are found. This indicates that objective outcomes of voice characteristics are not evidently related to self-perceived vocal dysfunction.

6.2 Recommendations

The current study is continued. Inclusion of patients is still carried on to increase sample size of the studied group. Furthermore longitudinal studies with large patient groups are recommended, to gain more insight in short- and long-term effects of the oncological treatment. The following recommendations can be taken into account in collecting and analyzing patient data. Comparison of objective and subjective outcomes are recommended to gain insight in voice characteristics, swallowing function and patients' experience. Analyzing sub-groups of patient characteristics in this heterogeneous group of early laryngeal cancer is recommended. Therefore precise reportage of localization and extension of the tumor as well as its resection has to be reassured. In analyzing acoustic voice characteristics, using data of running speech is recommended, this provides insights in a patients' natural way of voicing. The presumably deteriorated swallowing function is an undiscovered subject in the patient group of early laryngeal cancer. This deserves more attention.

The findings of the evaluated studies, this study and future research can lead to recommendations that ensure optimal preservation of function and maximization of HRQoL in early laryngeal cancer patients. It is assumed that cancer care can be improved. Clinicians will be able to indicate secondary problems as an effect of the tumor or its treatment in an early stage. Activities to improve the patients HRQoL, such as (preventive) rehabilitation, can be initiated. This increase in knowledge and the ability to anticipate can lead to advanced cancer care for early laryngeal cancer patients.

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