VOCAL FUNCTION EXERCISES AND VOCAL HYGIENE COMBINED TREATMENT APPROACH AS A METHOD OF IMPROVING VOICE QUALITY IN IRRADIATED PATIENTS FOR LARYNGEAL CANCERS

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ABSTRACT

Introduction*: Despite the negative effects of radiation therapy on voice quality is well documented in literature few studies have focused on the efficacy of voice therapy in the irradiated laryngeal cancers population. The purpose of this study was to investigate the efficacy of an evidence-based voice therapy, known as Vocal Function Exercises (VFE) in a combined approach with Vocal Hygiene (VH) in improving vocal function in patients who have been irradiated for laryngeal cancers and compared to the results of VH alone treatment.*

Materials and methods*: A prospective, randomized and controlled study involved patients with primary laryngeal cancer treated with curatively intended radiotherapy. Study group (10 patients) was treated with VFE+VH approach and control group (9 patients) was treated with a VH alone therapy; both interventions started one month following radiotherapy completion and lasted for 6 weeks. Voice Handicap Index (VHI) scores, laryngeal stroboscopy, high-speed laryngeal imaging, acoustic analysis, aerodynamic analysis, auditory-perceptual measures through the Grade, Roughness, Breathiness, Asthenia, Strain (GRBAS) rating scale and impact on Health-Related Quality of Life (HRQL) through the EORTC Quality of Life Questionnaire Head and Neck module (EORTC QLQ-H&N35) were evaluated at baseline and post-intervention.*

Results*: VFE+VH combined approach shows better and statistically significant improvement after vocal intervention when compared to VH alone group for VHI (p=0.023), GRBAS (p=0.038), MPT (p<0.001), jitter (p=0.015), NMWA (p=0.011), NGG (p=0.026) and EORTC QLQ-H&N35 (p=0.047).*

Conclusions*: The current investigation demonstrated that the VFE+VH combined approach was effective in improving the vocal function in irradiated patients with laryngeal cancers.*

Keywords*: voice therapy, laryngeal cancer, radiotherapy.*

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Introduction

Laryngeal cancer is the second most common head and neck cancer and constitutes 30% of all head and neck malignancies[1]. Well-known etiologic factors of laryngeal cancer include smoking, alcohol, human papilloma virus, radiation and gastric acid reflux[2,3].

The primary goal for treatment of laryngeal cancer is survival, but due to the important role in voice production and communication played by the larynx, organ preservation is increasingly desirable when considering treatment options[4]. Early laryngeal cancers are often treated with radiotherapy alone, while advanced laryngeal cancers are treated with a combination of radiotherapy and chemotherapy[5].

Surgical options may range from conservation surgery to total laryngectomy. However, this last is associated with significant morbidity since it results in a permanent mutilation of the natural source of voicing[6] and significant functional and psychologi-

cal sequelae which may create a negative impact on the quality of life of these individuals[7].

Consequently, following results from several studies, an increasing number of patients with laryngeal cancers have been treated primarily with radiation therapy, with or without chemotherapy, with the intent of preserving laryngeal structure and function[8]. However, preservation of structure through radiation therapy has not necessarily led to preservation of function. Several studies have demonstrated poor voice and swallowing outcomes as a result of radiation toxicity including excessive compensatory compression of laryngeal structures during phonation, which lead to significant abnormalities in vocal fold vibratory characteristics and impacting perceptual vocal quality[9], audioperceptual findings of hoarseness and persistent voice changes[10], increased perturbation and noise measures[11] and aerodynamic measures that reveal increased laryngeal airway resistance[12].

In this contest voice rehabilitation postradiation therapy assume relevant consideration and warrants attention. Unfortunately, there is a paucity of research with respect to voice rehabilitation in the irradiated population. Only a few studies have investigated the effects of voice therapy in postradiated laryngeal cancer patients[13].

A well-known evidence-based voice therapy is the Vocal Function Exercise (VFE) program, it includes a series of systematic voice exercises designed to strengthen and balance the laryngeal musculature, increase or improve vocal fold adduction, and coordinate the subsystems of voice production[14]. Although VFEs have been employed successfully in treating a variety of voice disorders, the efficacy of this approach for improving vocal function in patients who have undergone radiotherapy for laryngeal cancer has not been established.

The objective of the present study was to investigate the effect of VFE in a combined approach with VH on vocal function in adults irradiated for laryngeal cancers, comparing the results with the VH alone treatment.

The primary outcome measure was the change in pre- and post-intervention Voice Handicap Index (VHI) scores. Secondary outcome measures include laryngeal stroboscopy, high-speed laryngeal imaging, acoustic analysis, aerodynamic analysis, auditory-perceptual measures through the Grade, Roughness, Breathiness, Asthenia, Strain (GRBAS) rating scale and impact on Health-Related Quality of Life (HRQL) through the EORTC Quality of Life Questionnaire Head and Neck module (EORTC QLQ-H&N35)

Materials and methods

We carried out a prospective randomized controlled trial between June 2016 and November 2017 in the Otolaryngology Unit of the Santa Marta e Santa Venera Hospital in Acireale, Catania, Italy, after the approval by the ethical committee of the Unità Operativa Complessa (UOC) Otorinolaringoiatria - ASP 3 CT and the signed information consent by every patient.

The study involved patients with primary laryngeal cancer treated with curatively intended radiotherapy.

Inclusion criteria were adults over 18 years of age, previously irradiated for laryngeal cancer (with or without chemotherapy) at least 6 months prior to study participation and deemed cancer-free by the treating physician at the time of study recruitment, good cognitive abilities and adequate language competency in order to independently complete the questionnaires as well as participate in voice rehabilitation sessions. A presence of vocal fold paralysis or surface vocal fold pathology at the time of study recruitment constituted exclusion from the study. Subjects who met all of the inclusion criteria were then randomly allocated, using a statistical computing web programming (www.graphpad.com/quickcalcs), into two groups: an intervention group undergoing combining voice rehabilitation VFE+VH and a control group receiving only VH.

Voice interventions were conducted in line with a structured protocol by a certified speech-language pathologist not involved in this study and trained specifically in the care of patients with laryngeal cancer. Treatment plans started approximately one month following radiotherapy completion (baseline) and lasted for 6 weeks.

VH counseling involved educating and informing patients regarding factors that influence voice use and voice care. Sessions generally revolved around strategies that enhance and maintain vocal health according to standard practice(15), stressing hydration and dietary considerations since significant changes in salivary status and tissues are noted during this period.

VFE, as described by Stemple et al.[16], were designed to strengthen and rebalance the subsystems involved in voice production (i.e., respiration,

phonation, and resonance) through a program of systematic exercise. VFE is comprised of a series of four exercises which include a warm-up exercise, stretching, contraction and increased resistance exercises.

The VFE program for the proposed study lasted 6 weeks where the patient was required to perform the exercises twice a day, every day.

Outcome assessments as for all study patients occurred at the beginning of therapy (baseline) and after 6 weeks of treatment (post-intervention). Patient voice self-assessment were assessed by the VHI, developed by Jacobson et al.[17], this instrument, completed prior to and after voice treatment by the patients, permits an understanding of the handicapping nature of the voice disorder as perceived by the patient. Stroboscopic and high-speed laryngeal imaging examination was performed by a speech-language pathologist blinded to group assignment, using a digital video stroboscopy system with 70° rigid endoscope, XION EndoSTROB DX device (XION GmbH, Berlin, Germany) and DiVAS Version 2.8 software (XION GmbH, Berlin, Germany). Normalized mucosal wave amplitude (NMWA) and normalized glottal gap (NGG) were used as parameters of vocal fold vibratory function, they were measured by analyzing stroboscopic images during vocal fold vibration by the phonation of a sustained vowel at the patient's normal pitch and loudness[18].

Acoustic analyses evaluated jitter, shimmer using the DiVAS Voice Analysis (XION GmbH, Berlin, Germany) with a hand-held microphone. The aerodynamic assessment was examined with a phonation analyzer PA-500 (Nagashima Co., Osaka, Japan). Airflow measures were taken using an airflow mask and included a simple test of glottic efficiency as the maximum phonation time (MPT) which is the maximum time (in seconds) for which a person can sustain a vowel sound when produced on one deep breath and the mean flow rate (MFR) that is the average airflow passing through the glottis per second (ml/s). Auditory- perceptual assessment was independently evaluated by two speech-language pathologists blinded to group assignment through the GRBAS rating scale[19], which is scored from 0 to 3, where 0 = normal, 1 = slight impaired, 2 = moderate impaired, and 3 = severe impaired. The ratings of the five subscales were summed and the mean rating-score between two raters was calculated. The impact of voice vocal treatment plans on QoL was evaluated using the EORTC QLQ-H&N35. It was structurally made up of seven scales (pain, swallowing, sense, speech, social eating, social contact, and sexuality) and 11 single items that considered the most important clinical aspects characterizing the QoL in H&N cancer patients. It results in scales that score from 0 to 100. For the function scales, a score of 100 means perfect quality of life, whereas for the symptom scales it would indicate heavy burden. A change of ≥10 points can be considered a clinically relevant change[20].

In calculating sample size, the principal outcome measure was taken to be the VHI score[21].

If there was a difference in VHI (pre and post intervention) of 14.3 in the voice therapy group and 0.5 change in vocal hygiene group (assuming that the standard deviation is 11.6 units) and setting the significance level at 5% and sample power at 80%, a sample size of 16 subjects (8 in each group) would be required.

Statistical analysis

The results obtained in the present study were analyzed using the SPSS software version 20.0 (SPSS Inc., Chicago, IL, USA). Quantitative variables were presented as mean ± SD, whereas categorical variables as number and frequency. Comparisons for continuous variables between the two groups were performed using paired t-tests. Comparisons for non-continuous variables between the two groups were performed using the Wilcoxon signed-rank test. Statistical significance was set at $p<0.05$.

Results

A total of 21 patients eligible for inclusion in study were randomized into voice rehabilitation VFE+VH group (n=11) and control group receiving only VH (n=10). Two subjects, one belonging to the VFE+VH group and one to the VH only group, were lost to follow-up, so a total of 19 patients (10 for VFE+VH group and 9 for VH only group) were included in the final analysis. Patient demographic characteristics were generally similar between groups as shown in Table 1.

Significant improvement in each outcome was determined by comparing the baseline with after treatment scores for each treatment group as shown in Table 2 below. The extent of improvement of each domain was compared among the two treatment groups as evident in Table 3.

Characteristics	VFE+VH N=10	VH only N=9	Overall N=19	*p-value*
Age, in years				
Mean ± SD	68.4 ± 5.21	64.1 ± 7.18	40.7 ± 11.25	0.624
Median	61	60	39	-
Range	54-73	53-69	27-60	-
Gender, n (%)				
Male	8 (80.0)	8 (88.9)	16 (84.2)	0.831
Female	2 (20.0)	1 (11.1)	3 (15.8)	
Stage of the disease (TNM)				
T1N0M0	3 (30.0)	2 (22.2)	5 (26.3)	0.458
T2N0M0	4 (40.0)	3 (33.3)	7 (36.8)	0.512
T2N1M0	1 (10.0)	0 (0)	1 (5.3)	0.402
T3N0M0	2 (20.0)	4 (44.5)	6 (31.6)	0.509
Treatment type				
Narrow field irradiation	3 (30.0)	2 (22.2)	5 (26.3)	0.367
Wide field irradiation	6 (60.0)	7 (77.8)	13 (68.4)	354
Chemotherapy+ irradiation	1 (10.0)	0 (0)	1 (5.3)	0.293
Smoking status				
Non-smoker	2 (20.0)	3 (33.3)	5 (26.3)	0.486
Smoker	2 (20.0)	2 (22.2)	4 (21.1)	0.603
Quit smoking >12 m	6 (60.0)	4 (44.5)	10 (52.6)	0.328

Table 1: Patient demographic characteristics between groups.
*VFE: Vocal Function Exercises; VH: Vocal Hygiene; SD: standard deviation; *p < 0.05*

Patient self-assessment

Although VHI score was found to be reduced by VFE+VH and VH only, the change from baseline to after treatment was statistically significant only for the combining approach.

Auditory-Perceptual Ratings

GRBAS scale significantly improved in VFE+VH group after treatment (9.23±1.06 vs. 6.62±0.88; p<0.05), conversely, there was no statistically change in VH only group (8.88±0.86 vs. 8.12±0.74).

Health-related quality of life assessment

An overall improvement in EORTC QLQ-H&N35 was observed across both groups after 6 weeks of treatment.

However, further testing revealed that VFE+VH group had the highest increase of 5.40 as compared to 1.50 in VH only group (p =0.047).

Stroboscopic examination and high-speed parameters

NMWA and NGG significantly improved in VFE+VH group after treatment (5.03 and -1.23, respectively). The VH only group did not show any statistically pre-post changes in these parameters (0.23 and - 0.21, respectively).

	VFE+VH N=10		VH only N=9	
Subjective Outcomes	**Baseline**	**After treatment**	**Baseline**	**After treatment**
VHI	38.45 ± 11.16	**30.22 ± 8.19***	27.69 ± 10.14	25.43 ± 9.47
GRBAS	9.23 ± 1.06	**6.62 ± 0.88***	8.88 ± 0.86	8.12 ± 0.74
EORTC QLQ-H&N35 (overall)	48.45 ± 12.55	53.85 ± 11.45*	50.15 ± 10.15	51.65 ± 10.45
Objective Outcomes				
NMWA (units)	5.63 ± 2.35	**10.66 ± 4.65***	6.02 ± 2.16	6.25 ±2.21
NGG (units)	1.48 ± 1.87	**0.25 ± 0.05***	1.43 ± 1.16	1.22 ± 1.08
Jitter (%)	1.46 ± 1.17	**0.68 ± 0.34***	1.73 ± 0.65	1.66 ± 0.48
Shimmer (%)	2.74 ± 1.88	2.15 ± 0.99	2.18 ± 1.76	2.04 ± 1.54
MPT (sec)	13.51 ± 4.84	**19.73 ± 3.85***	18.54 ± 4.55	17.67 ± 3.62
MFR (ml/sec)	161.23±37.52	164.14±35.84	155.16±28.47	163.75±29.33

Table 2: Subjective and objective outcomes at baseline and after treatment in the two study groups.
*VFE: Vocal Function Exercises; VH: Vocal Hygiene; VHI: Voice Handicap Index; GRBAS: Grade, Roughness, Breathiness, Asthenia, Strain; EORTC QLQ-H&N35: EORTC Quality of Life Questionnaire Head and Neck module; NMWA: Normalized mucosal wave amplitude; NGG: normalized glottal gap; MPT: maximum phonation time; MFR: mean flow rate; *p < 0.05*

Acoustic Analysis

Jitter significantly improved in VFE+VH group (1.46±1.17 vs. 0.68±0.34), but there was no statistically significant change in VH only group (1.73±0.65 vs. 1.66±0.48). Despite the slight decrease in shimmer, no significant change was observed neither in pre-post values for both groups nor between the two groups (p=0.077).

Aerodynamic assessment

MPT significantly increased in VFE+VH group (13.51±4.84 vs. 19.73±3.85). On the contrary, a slight decrease was detected in patients in VH only group, although, no statistically significant (18.54±4.55 vs. 17.67±3.62). No significant change was observed neither in pre-post values for both

groups nor between the two groups (p=0.077). No significant change in MFR was observed in the VFE+VH and VH only group after 6 weeks of treatment or between the two groups (p=0.102).

	VFE+VH N=10	VH only N=9	p-Value
Subjective Outcomes			
VHI	-8.23	-2.26	0.023*
GRBAS	-2.61	-0.76	0.038*
EORTC QLQ-H&N35 (overall)	5.4	1.5	0.047*
Objective Outcomes			
NMWA (units)	5.03	0.23	0.011*
NGG (units)	-1.23	-0.21	0.026*
Jitter (%)	-0.78	-0.07	0.015*
Shimmer (%)	-0.59	-0.14	0.077
MPT (sec)	6.22	-0.87	<0.001*
MFR (ml/sec)	2.91	8.59	0.102

Table 3: Mean change in scores by treatment group.
*VFE: Vocal Function Exercises; VH: Vocal Hygiene; VHI: Voice Handicap Index; GRBAS: Grade, Roughness, Breathiness, Asthenia, Strain; EORTC QLQ-H&N35: EORTC Quality of Life Questionnaire Head and Neck module; NMWA: Normalized mucosal wave amplitude; NGG: normalized glottal gap; MPT: maximum phonation time; MFR: mean flow rate; *p < 0.05*

Discussion

Voice rehabilitation interventions following radiotherapy for laryngeal cancer have been scarcely addressed in previous studies. Traditionally, VH approaches are the most commonly used intervention method for voice rehabilitation in this population. Studies in this context have reported improvements in VHI scores for patients irradiated for early glottic cancers following VH interventions[21], a beneficial effect on the mean VHI, percent jitter, and shimmer also after more than one year of follow-up[22], a significant improvements in voice quality and self-rated vocal function[23] and a greater improvement on patient's self-perception of vocal quality with no functional decline in vocal roughness 6-12 months post radiation therapy as a result of VH than the control group[10].

Voice rehabilitation, in studies reported above, included vocal hygiene with non-specified voice and breathing exercises compared to a control group which generally, did not receive any voice treatment.

The present study was designed to investigate the effectiveness, in improving vocal function in adults irradiated for laryngeal cancers, of a specific voice therapy approach, the VFE. VFEs are a set of laryngeal manipulations which are aimed at strengthening and rebalancing the three subsystems of voice production[16]. To date, several studies have demonstrated the efficacy of VFEs in different situation like elite voice users, normal voices, pathological voice disorders and elderly people[14, 24-27] but, the efficacy of VFEs in patients irradiated for laryngeal cancers has poorer studied.

To this end, the present study compared the efficacy of VFE + VH combined treatment to VH treatment alone in improving vocal function using perceptual ratings (GRBAS), aerodynamic assessment (MPT, MFR), acoustic analysis (jitter, shimmer), vibratory analysis (NMWA, NGG), VHI, and the impact of voice vocal treatment on QoL (EORTC QLQ-H&N35). Although MFR and shimmer didn't change significantly between the two groups, the present study indicated significant improvements in GRBAS, MPT, jitter, NMWA, NGG, VHI and EORTC QLQ-H&N35 after the combined approach compared with the VH alone treatment.

Our results support previous findings which have demonstrated improvements in voice-related quality of life and auditory perceptual measures of voice as a result of voice therapy interventions following radiation

therapy for laryngeal cancers[10,21-23]. Moreover, our experience adds further support to the evidence that VH is more effective when paired with a more physiologic voice therapy approach, the VFE, as reported by previous studies[14,28]. Trying to explain our results from a theoretical point of view we can say that VFEs have proved to be effective in improving vocal function, slowing down or nullify post-radiotherapy injury, facilitating activity-dependent plasticity, oxidative metabolic capacity and quantity of neuromuscular junctions through vocal exercise stimulation as noted in some experimental studies[29], improving in this way vocal fold vibratory function.

Our study has some limitations. The measurement of the NMWA and NGG is affected by different conditions of pitch, loudness and compensatory activity of extrinsic muscles so this may lead to bias in the estimation of their values. We attempted to correctly and consistently obtain NMWA and NGG by taking measurements during vocal fold vibration

at the patient's normal pitch and loudness, and by using images taken at the identical position of the glottis at resting condition. Compliance with the voice training between the sessions was not assessed; this could provide insight into the matter of success of combined voice rehabilitation.

Conclusions

Although future studies are needed to confirm the results of this investigation, our data suggest that VFE is a useful treatment for improving vocal function in irradiated population for laryngeal cancers.

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