Volume 21, No 2 | International Journal of Radiation Research, April 2023

Long-term study of vocal dysfunction and quality of life in patients with non-laryngeal head and neck cancers post chemo-radiation therapy: Results of prospective analysis

P. Fadavi[1], S. Bagherzadeh[2*], F. Torabinezhad[3], F. Goli-Ahmadabad[4], M. Beiki[5], S. Bijari[6], S. Sayfollahi[7], Z. Momeni[2]

[1]*Department of Radiotherapy, School of Medicine, Iran University of Medical science, Tehran, Iran*
[2]*Medical Physics Department, School of Medicine, Isfahan University of Medical Science, Isfahan, Iran*
[3]*Department of Speech & Language Pathology, School of Rehabilitation Sciences, Iran University of Medical Sciences, Tehran, Iran*
[4]*Department of Medical Physics, School of Medicine, Iran University of Medical Science, Tehran, Iran*
[5]*Department of Radiation Oncology, Shohadaye Haftom-e-Tir Hospital, Iran University of Medical Sciences, Tehran, Iran*
[6]*Department of Medical Physics, Faculty of Medical Sciences, Tarbiat Modares University, Tehran, Iran*
[7]*Department of Neurosurgery, Faculty of Medical Sciences, Iran University of Medical Sciences, Tehran, Iran*

► ***Original article***

***Corresponding author:**
Sakineh Bagherzadeh, Ph.D.,
E-mail:
sakineh.bagherzadeh@yahoo.com

Received: July 2022
Final revised: September 2022
Accepted: November 2022

Int. J. Radiat. Res., April 2023; 21(2): 227-232

DOI: 10.52547/ijrr.21.2.7

Keywords: *Quality of life, radiation therapy, non-laryngeal cancers, voice evaluation.*

ABSTRACT

***Background*:** Vocal problems caused by Chemo-radiation therapy (CRT) can affect a patient's quality of life (QOL) for a long time. This study aims to follow up and evaluate the voice of Persian-speaking patients with non-laryngeal head and neck cancer up to eighteen months after treatment. ***Material and Methods*:** This prospective study was conducted to assess the voice of disease-free patients with various head and neck malignancies treated with CRT. The voice assessment was conducted at four points: before, at the end of treatment, and six and eighteen months after treatment. At the time of the last assessment, there were only 30 patients with an average age of 48.86±14.89 and in the range of (18-75) years. For a comprehensive assessment, acoustic, expert-rater, and subjective evaluation of voice was conducted. The Pearson correlation coefficient for all acoustic parameters, subgroups of the Persian VHI-30 questionnaire, and perceptual measurements were computed. The effect of essential factors on patient QOL associated with the voice in different groups was examined. ***Results*:** All acoustic parameters, other than fundamental and habitual frequencies, subjective and perceptual data values increased significantly ($P < 0.001$) during the treatment and decreased at the last assessment. None of the values have returned to pre-treatment levels. There was a significant relationship between some acoustic parameters, Persian VHI-30 questionnaire values, and G on the GRBAS scale. Chemotherapy and smoking were influential factors in patients' QOL. ***Conclusions*:** Vocal problems and reduced voice related QOL in patients treated with CRT may persist for years after treatment.

INTRODUCTION

Chemo-radiation therapy (CRT), along with surgery and radiation therapy, is one of the main methods of treating head and neck cancers that target tumor cells [1, 2]. In the patients with non-laryngeal head and neck cancers, the normal larynx in the absence of malignancy may be exposed to high radiation doses [3, 4]. Radiation causes vocal cord dysfunction, incomplete glottis closing, pharyngeal dryness and erythema. These complications increase patients' complaints about their voices compared to the pre-treatment [1- 4].

Voice disorders affect patients' communication and emotions and, eventually, reduce their voice-related quality of life (QOL) [2, 5, 6]. One of the most critical challenges after radiation therapy is to assess and maintain the patient's QOL [1]. Voice is a multiple-dimensional phenomenon. Each evaluation method measures just one particular aspect of vocal function. Therefore, multiple methods should be used for the overall evaluation [7].

Well-known methods of voice examination are include acoustical analysis of voice signals by the software [5, 6], self-assessment by the patient use of questionnaires [7-11] and perceptual evaluation by experienced speech therapists [12-14]. Although various voice evaluation methods differ in implementation, appropriate and significant relationships have been observed between a number of components and their parameters [12, 13, 18-20].

Examining and evaluating the quality of voice post

[DOI: 10.52547/ijrr.21.2.7]

CRT are essential issues and various studies have been conducted in this regard [20-23]. In head and neck cancers, swallowing and voice complications are the most common damages after CRT. However, compared to other problems, the evaluation of vocal problems and their effect on the patient's QOL has been poorly described in earlier studies [7, 10, 15]. There is an increase in the life expectancy in cancerous patients after the treatment. This issue makes it necessary to study patient's problems for a long time. Various studies have investigated larynx function and voice problems using various methods of voice assessment [7, 21, 23-25]. Another group of studies have examined the relationship between different assessment methods [14, 19, 20].

Little is known about the patient's QOL related to voice, particularly for Iranian patients with non-laryngeal head and neck cancers. There are differences in vowel systems between the Persian and English languages, and acoustic factors should differ due to different phonetic patterns [18]. Our team has already focused on voice problems in these patients six months after CRT.

The goal of this study was to conduct a longer follow-up to assess the QOL related to voice in remaining disease-free patients of our original patients up to eighteen months post-treatment and, then, assess the relationship between the objective and subjective voice evaluation methods. To the best of our knowledge, this is the first long-term study for investigating radiation-induced laryngeal damage and vocal dysfunction in Persian-speaking patients with non-laryngeal head and neck cancers.

MATERIALS AND METHODS

Thirty patients with squamous cell carcinoma of head and neck cancers were proven by (imaging and biopsy) with no malignancy in the larynx, a survivor from the previous study signed the consent form and entered this study. The study was carried out over three years, between December 2018 and September 2021. All the procedures carried out in this study were in accordance with the ethical standards of the responsible committee on human experimentation and compliance with the 1975 Helsinki Declaration and its later amendments. All the patients were treated with radiation therapy or CRT at the Tehran Hafte Tir Hospital. All the patients with laryngeal invasive, laryngeal or thyroid surgery, voice disorders and vocal pathology were excluded from the study. Eighty normal individuals who were adjusted in age, gender and smoking status were considered a control group.

Treatment protocol

At first and before the treatment, computed tomography (CT) (CT, Siemens, Germany) was performed in the treatment position according to a standardized CT acquisition protocol with a 3mm slice thickness. For each patient, the larynx as a normal organ was contoured under the supervision of an experienced radiation oncologist. After dose calculations, differential dose volume histograms (DVHs) were calculated and the mean dose delivered to the larynx was determined.

All the patients were treated with 3-D conformal radiation therapy (3D-CRT) by 46–70 Gy in 23–35 fractions and a dose per fraction of 1.8 or 2 Gy for 5 consecutive days per week. Some of the patients underwent concurrent CRT by receiving (40 mg/m2) Cisplatin (Bristol Myers Squibb, United *States*) on the weekly basis.

Voice assessment

Voices of all the patients were assessed at four-time points: at baseline, end of treatment and six and eighteen month's post-treatment. To make a comprehensive assessment, quantitative (acoustic analysis) and qualitative (assessment by questionnaire and expert rater) aspects of voice were evaluated.

Objective and subjective voice assessment

In a soundproof room, each patient sat comfortably on a chair with a 7-10 cm microphone-to-mouth distance. The patients were instructed to sustain the vowel /a/ for at least 5sec, count numbers from 1 to 10, and then read the Persian text of "pedarbozorg." This text was developed to assess voice samples in Iranian patients with vocal dysfunctions [16].

The voice recordings were made at the sampling frequency of 44.1 kHz with 16 bits per sample.

The recorders were transferred to a wave format computer; three seconds of vowel /a/ and the whole time of other recorded voices were selected. Then, acoustic parameters were extracted.

Acoustic analysis was done using the PRAAT software (version 6.0.25). The voices were recorded by the zoom (H5, Japan) recorder [17].

One of the appropriate tools that have been designed to evaluate the QOL related to voice through patient self-assessment is the voice handicap index-30 (VHI-30) questionnaire. This questionnaire has 30 questions in three subgroups; VHI-Physical (VHI-P), VHI-Functional (VHI-F) and VHI-Emotional (VHI-E). Each subgroup has 10 questions and each question is rated from zero to 4 scores. The total score of the questionnaire is 120. For the Persian VHI-30 questionnaire, a total score of 14.5 or higher is considered abnormal [18, 19]. All the participants were instructed to complete the Persian VHI-30 questionnaire.

All the patients read the standard text of the "Pedarbozorg". Perceptual evaluation of vocal disorders using the GRBAS scale consisting of the (grade, roughness, breathiness, asthenia and strain) scale was performed by the speech-language

[DOI: 10.52547/ijrr.21.2.7]

pathologist using a 4-point grading system; (0-4: normal, mild, moderate and severe).

Our study was conducted on Persian-speaking patients; a Persian VHI-30 questionnaire and a Persian text were used for the perceptual and qualitative evaluation.

Statistical analysis

Pre-and post-treatment results were carried out using a one-way ANOVA test. Descriptive analysis was used for reporting the means ± standard deviation of all the variables. Independent samples *t*-test was performed to evaluate the effects of chemotherapy, radiation dose and smoking on the patient's QOL related to voice. Due to the normal distribution of data, Pearson's correlation tests were performed to find out any possible relationship between patients' scores on the Persian VHI-30 questionnaire, acoustic variables and the GRBAS scale scores. The statistical analysis was conducted in SPSS software Version 26.0, and the *P* value of <0.05 was considered significant.

Interpreter agreement for GRBAS rating between the two experienced experts was measured using the intra-class correlation coefficient.

RESULTS

Survivors and disease-free individuals to further follow up agreed to enter this study. At eighteen months post-treatment, out of seventy patients at the start point (before the treatment), only thirty patients, including 20 men and 10 women with the mean age of 48.86±14.89 and range of (18-75), were remained. The remaining patients had malignancies in different areas of the head and neck (table 1).

The pre-treatment data of these patients were compared with the control group data. There was no significant difference between their results (P>0.05) [20].

Table 1. Patients Demographics Data.

Non-laryngeal Patients	Frequency (%)
Number of patients	30 (100%)
Mean age (range)	48.86±14.89 (18-75)
Males Females	20 (66.6%) 10 (33.3%)
Site of tumors Nasopharyngeal Oral Cavity Non-Hodgkin lymphoma Parotid	 10 (33%) 11 (36%) 5 (16.6%) 4 (13.3%)
Smoking status Males Females	 16 (80%) 1 (10%)
Types of treatment Radiation therapy Chemo-radiation therapy (CRT)	 15 (50%) 15 (50%)

One-way ANOVA test was performed for the patients' group from baseline to eighteen months post-treatment. As can be seen, the fundamental and habitual frequencies for the males (P=0.148, P=0.195) and females (P=0.346, P=0.332) did not show significant changes compared to the baseline. However, other acoustic parameters included jitter (local (%), perturbations of frequency, P=0.003), shimmer (local (%), perturbations of amplitude, P=0.039), noise to harmonic ratio (NHR, P=0.040) and harmonic to noise ratio (HNR, P=0.006), scores of the Persian VHI-30 questionnaire subgroups including (VHI-E, VHI-F, VHI-P; P<0.001) and perceptual evaluation measures of G showed significant changes (P<0.001; table 2).

Table 2. Voice evaluation based on acoustic analysis, Persian VHI-30 questionnaire, and expert rater from baseline to eighteen months after treatment, Mean ± SD were calculated for each parameter (numbers of patients=30).

Timeline / Voice assessment	baseline	End of treatment	Six months after treatment	Eighteen months after treatment	P-value
Acoustic parameters					
Fundamental Frequency (male)	118.32± 13.28	132.30± 28.86	124.22± 30.93	117.65± 6.69	0.148
Habitual pitch (male)	124.30± 12.43	130.09± 15.21	127.20± 6.44	123.11± 7.63	0.195
Fundamental Frequency (female)	178.83± 10.15	189.27± 5.02	183.63± 22.71	180.86± 9.24	0.346
Habitual pitch (female)	180.50± 6.29	186.07± 10.23	180.91± 11.34	177.82± 11.38	0.332
Jitter (local)%	0.44± 0.09	0.53± 0.08	0.48±0.11	46± 0.07	0.003*
Shimmer (local)%	2.84± 1.87	3.72± 1.23	3.01±1.06	2.65± 1.69	0.039*
NHR	0.013± 0.015	0.023± 0.017	0.015±0.015	0.014± 0.011	0.040*
HNR	19.45± 1.30	18.65± 1.57	19.79± 1.41	19.65± 1.03	0.006*
VHI-30 subgroups					
VHI-F	1.23± 1.07	7.63± 2.98	5.53± 2.11	3.77± 1.54	<0.0001*
VHI-E	0.73± 0.90	6.43± 2.59	3.80± 1.21	3.17± 1.23	<0.0001*
VHI-P	1.50± 1.04	10.67± 3.62	6.77± 2.66	5.47± 2.12	<0.0001*
VHI-T	3.50± 2.17	24.63± 7.49	16.10± 4.95	12.33± 4.35	<0.0001*
GRBAS scale					
G	0.47± 0.50	1.43±1.16	0.83±0.95	0.5±0.77	<0.0001*

NHR: Noise to Harmonic Ratio, HNR: Harmonic to Noise Ratio, VHI-F: Voice Handicap Index-Functional subgroup, VHI-E: Voice Handicap Index-Emotional subgroup, VHIP: Voice Handicap Index-Physical subgroup, VHIT: Voice Handicap Index-Total subgroup, G: Grade. *Significant difference in P<0.05, Result from descriptive analysis and One-way Anova test.

The trend of changes in jitter, shimmer, fundamental and habitual frequencies and NHR parameters increased from baseline to the end of treatment. They then decreased at six and eighteen months post-treatment. Variations in the HNR parameter are indicated in the opposite direction.

Based on the independent samples *t*-test, it was observed that the values of the three VHI-30 subgroups were significantly increased in the

[DOI: 10.52547/ijrr.21.2.7]

patients who received CRT and those with a history of smoking (P<0.05), compared to the other group who only received radiotherapy and were non-smokers (P>0.05). There were no significant changes in the scores of the Persian VHI-30 questionnaire subgroups in the patients with a mean laryngeal dose higher or lower than 44 Gy (P>0.05). The details and exact values of P are given in table 3.

Table 3. Assessment the impact of important factors on the voice and patient's QOL based on the Persian VHI questionnaire subgroup scores. Chemo-radiation therapy (CRT) and Smoking are important factors.

Variables		VHI-30 subgroup			
		VHI-F	VHI-E	VHI-P	VHI-T
Chemo-Radiation Therapy (CRT)	yes	6.48±2.73	4.81±2.19	8.76±3.60	19.89±7.39
	no	4.59±2.33	2.04±2.32	5.94±2.90	14.39±7.02
	p-value	0.04*	0.001*	0.012*	0.003*
Mean dose	>44 Gy	6.33±2.75	4.88±2.30	8.49±3.67	19.67±7.69
	<44Gy	5.95±2.39	3.76±2.09	7.15±3.01	17.27±6.50
	p-value	0.09	0.081	0.26	0.18
Smoking	yes	5.14±3.43	4.07±2.87	6.92±4.19	16.17±1.14
	no	3.67±2.35	2.76±1.89	4.92±3.78	11.20±7.49
	p-value	0.006*	0.003*	0.008*	0.002*

VHI-F: Voice Handicap Index-Functional subgroup, VHI-E:Voice Handicap Index-Emotional subgroup, VHIP: Voice Handicap Index-Physical subgroup, VHIT: Voice Handicap Index-Total subgroup. *Significant difference in P<0.05, Results from Independent samples t-test.

The results of Pearson's correlation coefficient for acoustic parameters, Persian VHI-30 questionnaire subgroups and perceptual evaluation based on the GRBAS scale were calculated.

Grade (G) on the GRBAS scale showed a positive and mild relationship with fundamental frequency (r=0.316, P<0.05) and jitter (local %) (r =0.350, P<0.05) and a negative relationship with HNR (r=-0.298, P<0.05). Three subgroups of the Persian VHI-30 questionnaire including VHI-F (r= 0.646, P<0.01), VHI-E (r=0.378, P<0.05), VHI-P (r= 0.563, P<0.01) and VHI-T (r=0.601, P<0.01) showed a moderate relationship with G.

For acoustic parameters and the PersianVHI-30 questionnaire, there was a correlation between jitter (local) % with VHI-E (r=0.468, P<0.01) and VHI-T (r=0.455, P<0.05), and a mild correlation between the habitual frequency with VHI-T (r = 0.451, P <0.05). Results are shown in table 4.

The frequency of damaged patients from all the voice evaluation methods was calculated in the final evaluation. As observed, the percentage of damaged patients at the end of the treatment in all three methods was high. Gradually, in the six and eighteen months post-treatment, these values decreased, but did not reach zero (figure 1).

DISCUSSION

Radiation therapy has many acute and late side effects. In the patients with non-laryngeal head and neck cancers, the larynx as a normal organ can be affected by radiation. The radiation dose to the

Table 4. Correlation between Acoustic parameters and Persian VHI -30 questionnaire subgroups and G on the GRBAS in eighteen months post-treatment.

Time	Acoustic variables with VHI-30 questionnaire & Grade of GRBAS					
Eighteen months Post-treatment	Acoustic parameters	VHI-F	VHI-E	VHI-P	VHI-T	G
	F0 (Hz)	0.164	0.180	0.128	0.192	0.316*
	Habitual pitch (Hz)	0.174	0.263	0.193	0.457*	0.126
	Jitter (local)%	0.373	0.468**	0.360	0.455*	0.350*
	Shimmer (local)	0.01	0.095	0.134	0.085	0.046
	NHR	0.100	0.04	0.134	0.01	0.135
	HNR	-0.114	-0.111	-0.103	-0.097	-0.289*
	VHI-30 questionnaire with GRBAS scale					
	Grade of GRBAS	VHI-F	VHI-E	VHI-P	VHI-T	
	G	0.646**	0.378*	0.563**	0.601**	

VHI-F: Voice Handicap Index-Functional subgroup, VHI-E:Voice Handicap Index-Emotional subgroup, VHIP: Voice Handicap Index-Physical subgroup, VHIT: Voice Handicap Index-Total subgroup, G: Grade. Results from Pearson Correlation coefficients. *Correlation is significant at the 0.05 level (2-tailed). ** Correlation is significant at the 0.01 level (2-tailed).

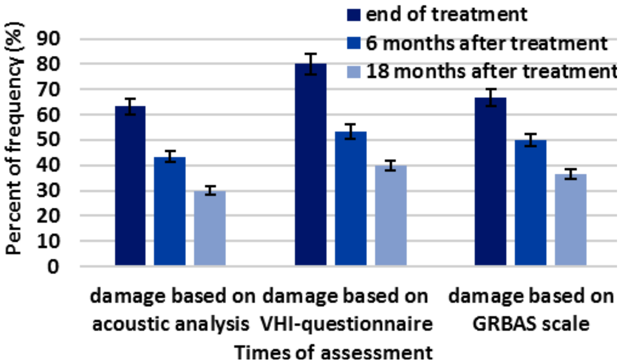

Figure 1. The percent of frequency for damaged patients with vocal dysfunction at three-time points: the end of treatment, six and eighteen months after the end of treatment based on acoustic analysis, Persian VHI questionnaire, and perceptual evaluation based on the GRBAS scale. The error bar shows the percentage.

larynx causes damage to laryngeal salivary tissue, leading to xerostomia and affecting vocal performance, which can happen either soon or late [3, 15, 21-23]. Vocal disorders or dysphonia, with its negative impact on communication and QOL, is undoubtedly one of the severe side effects, which has been underestimated in many cases [7, 8, 13].

In this study, we investigated three important issues: first, voice evaluation of the patients eighteen months post radiation treatment using perceptual and instrumental methods; secondly, assessment of dosimetric and clinical factor's effects on the incidence and severity of vocal problems; finally, investigating the relationship between GRBAS scale, VHI-30 score and objective acoustic measures.

In our previous study, voice evaluation was assessed from the baseline until six months post-treatment. Our results showed that the values of acoustic parameters and scores of the Persian VHI-30 questionnaire were increased significantly compared to the pre-treatment data and the patients complained about their vocal function [20]. For further

[DOI: 10.52547/ijrr.21.2.7]

investigations, we followed the thirty survivor patients up to eighteen months post-treatment. Our newer results showed that the values of acoustic parameters, perceptual measurements based on the GRBAS scale and Persian VHI-30 questionnaire scores had significant changes from the pre-treatment data again.

Increasing acoustic parameter values, VHI-30 questionnaire scores and G on the GRBAS scale during the treatment confirmed acute lesions such as edema. Laryngeal edema is acute damage that occurs at doses over 44 Gy [24] and usually resolves several months after treatments [4, 23]. On the other hand, chronic radiation-related complications, such as fibrosis, persist and change the vibration pattern of the vocal cords and affects the patient's quality of voice [1, 21, 22]. Values of some acoustic parameters probably approach the baseline value several months post-treatment, but the changes and decreases in voice quality from the patient's perspective and based on experts-rater remain years after the treatment [21].

Another important issue was to investigate the effect of various factors on aggravating the radiation-induced side effects. To carry out this evaluation, the Persian VHI-30 questionnaire was used. This questionnaire is a powerful tool for assessing voice-related QOL. A higher score on the VHI-30 questionnaire indicates better patient knowledge of vocal problems [7]. Various factors such as age, gender, chemotherapy, smoking and mean laryngeal dose can be involved in the occurrence of laryngeal damage and vocal dysfunction [25].

The survivor patients were present with different types of tumors, age, gender and smoking history, treated with radiation or concomitant CRT. Therefore, the total prescribed dose and the mean laryngeal dose differed for each individual. Results of the Persian VHI-30 questionnaire in the previous study showed that chemotherapy, mean laryngeal dose and smoking habits could reduce voice quality [20]. In the current study, significant changes were seen only in the patients who received concomitant CRT and had the smoking history. Indeed, it should be noted that some patients under their physician's supervision had started smoking within a year post-treatment and were smoking during this evaluation. Adding chemotherapy to radiation therapy creates a synergistic effect between both treatments. Chemotherapy has a beneficial effect on treating tumor tissue, but can also cause damage to irradiated tissues, including the larynx [26]. In contrast to the previous study, the results for patients who received mean laryngeal doses above 44 Gy were not significantly different from the other patients. As mentioned above, laryngeal edema from radiation exposure is acute and transient damage that eliminates approximately one year after treatment [23].

It has already been observed that there are relationships between some acoustic parameters and subgroups of the Persian VHI-30 questionnaire at different evaluation times [20]. At eighteen months post-treatment, the results were almost consistent with the results of the earlier studies [9, 20, 27-30]. Niebudek-Bogusz et al. investigated relationships among English-speaking teachers with dysphonia. They showed positive and moderate relationships between all the acoustic parameters and subgroups of the VHI-30 questionnaire [28]. In another study, Schindler et al. evaluated the correlation between the VHI-30 questionnaire and acoustic analysis in four groups of patients with different origins of dysphonia. They concluded the correlation between the VHI-30 subgroup's score and some acoustic parameter increased in the populations with vocal dysfunction of the same origin [9]. Our results in this study for acoustic parameters and VHIT -30 subgroups were in agreement with those of the mentioned studies.

In our study, all scores of VHI-30 subgroups had a positive relationship with the G value. Considering that the G provides reliable, accurate and stable results, it can reflect the severity of vocal problems [19]. So, in this study, only G was considered. Davies-Husband *et al.* [21] showed that although the acoustic parameters return to the baseline state, based on the patient's judgment of their voice and the progress of experts, the patients still suffer from vocal problems.

A positive and moderate correlation between the G and all subgroups of the Persian VHI-30 questionnaire in this study can confirm this issue. Brinton *et al.* concluded the positive and strong relationship between all the vocal parameters in the three voice evaluation methods [31]. Our results in this study were in line with their findings.

The purpose of following-up the patients during and post treatment was to investigate the radiation-induced vocal disorders in their communication interaction and mental conditions. Instrumental and qualitative evaluations of voice were performed at four-time points. At each mentioned time, the impact of radiation dose, side effects of chemotherapy and other acute and late complications caused by the radiation treatment on the patient's quality of voice were studied and a proper perspective of the treatment was observed.

Our results showed that vocal problems caused by radiation therapy may persist for months or years after the end of treatment and affect the patient's QOL.

Finally, the use of locoregional treatments such as tomotherapy and intensity-modulated radiation therapy (IMRT) to reduce the typical tissue complications near the tumor, quit smoking and refer to rehabilitation specialists during and after the treatment had been suggested to improve and maintain the QOL.

[DOI: 10.52547/ijrr.21.2.7]

CONCLUSIONS

This study concluded that chronic complications caused by CRT in the patients with non-laryngeal head and neck cancers affect and reduce the patient's QOL related to voice for several months or years post -treatment. Voice evaluation methods based on acoustic analysis, use of questionnaires and evaluation by experts can still be capable and accurate in diagnosing vocal problems.

ACKNOWLEDGEMENTS

The authors would like to acknowledge the staff of radiation therapy Department at the Hafte Tir Hospital, Tehran, Iran, for their good cooperation.

Conflict of interest: All authors declare no competing interests.

Ethical approval: All procedures performed were in accordance with the ethical standards of the institutional and/or national research committee and with the 1975 Helsinki Declaration and its later amendments.

Informed consent: Informed consent was obtained from all participants included in the study.

Funding: None.

Author contribution: P.F., contributed and conducting the study, and agreed for all aspects of the work. S.B, contributed in the conception of the work, contributed in the writing, editing and revising the draft, approval of the final version of the manuscript and agreed for all aspects of the work. F.T., contributed and conducting the study, and agreed for all aspects of the work. F. GA., contributed and conducting the study, and agreed for all aspects of the work. M.B. contributed and conducting the study, and agreed for all aspects of the work. S.B., contributed and conducting the study, and agreed for all aspects of the work. S. S., contributed and conducting the study, and agreed for all aspects of the work. Z. M., contributed and conducting the study, and agreed for all aspects of the work.

REFERENCES

1. Sreenivas A, Sreedharan S, Narayan M, *et al.* (2021) Effect of vocal rehabilitation after chemoradiation for non-laryngeal head and neck cancers. *Acta Otorhinolaryngologica Italica, **41**(2): 131-141*.
2. Mostaghimi H, Ahmadabad FG, Rezaei H (2021) Super-selective intra-arterial platinum-based chemotherapy concurrent with low-dose-rate plaque brachytherapy in the treatment of retinoblastoma: A simulation study. Journal of Cancer Research and Therapeutics, ***17**(1): 130-136*.
3. Sagiroglu S and Kurtul N (2020) The effect of supraclavicular radiotherapy on acoustic voice quality index (AVQI), spectral amplitude and perturbation values. *Journal of Voice, **34**(4): 649. e7-. e13*.
4. Fung K, Yoo J, Leeper H, Hawkins S, Heeneman H, Doyle PC, *et al.* (2001) Vocal function following radiation for non-laryngeal versus laryngeal tumors of the head and neck. *The Laryngoscope, **111** (11): 1920-4*.
5. Brockmann M, Drinnan MJ, Storck C, Carding PN (2011) Reliable jitter and shimmer measurements in voice clinics: the relevance of vowel, gender, vocal intensity, and fundamental frequency effects in a typical clinical task. *Journal of voice, **25**(1): 44-53*.
6. Vaziri G, Almasganj F, Behroozmand R. (2010) Pathological assessment of patients' speech signals using nonlinear dynamical analysis. *Computers in Biology and Medicine, **40**(1): 54-63*.
7. Kraaijenga S, Oskam I, Van Son R, *et al.* (2016) Assessment of voice, speech, and related quality of life in advanced head and neck cancer patients 10-years+ after chemoradiotherapy. *Oral oncology, **55**: 24-30*.
8. Maertens K and De Jong F (2007) The voice handicap index as a tool for assessment of the biopsychosocial impact of voice problems. *B ENT, **3**(2): 61-6*.
9. Schindler A, Mozzanica F, Vedrody M, *et al.* (2009) Correlation between the Voice Handicap Index and voice measurements in four groups of patients with dysphonia. *Otolaryngology-Head and Neck Surgery, **141**(6): 762-9*.
10. Van der Molen L, van Rossum MA, Jacobi I, *et al.* (2012) Pre-and posttreatment voice and speech outcomes in patients with advanced head and neck cancer treated with chemoradiotherapy: expert listeners' and patient's perception. *Journal of Voice, **26**(5): 664. e25-. e33*.
11. Woisard V, Bodin S, Yardeni E, Puech M (2007) The voice handicap index: correlation between subjecti ve patient response and quantitative assessment of voice. *Journal of Voice, **21**(5): 623-31*.
12. Hamdan A-l, Geara F, Rameh C, *et al.* (2009) Vocal changes following radiotherapy to the head and neck for non-laryngeal tumors. *European Archives of Oto-Rhino-Laryngology, **266**(9): 1435-9*.
13. Jalalinajafabadi F, Gadepalli C, Ascott F, *et al.* (2017) Perceptual evaluation of voice quality and its correlation with acoustic measurement. *European Modelling Symposium, 107-111*.
14. Nemr K, Simoes-Zenari M, Cordeiro GF, *et al.* (2012) GRBAS and Cape-V scales: high reliability and consensus when applied at different times. *Journal of voice , **26**(6): 812. e17-. e22*.
15. Kraaijenga SA, van der Molen L, Jacobi I, *et al.* (2015) Prospective clinical study on long-term swallowing function and voice quality in advanced head and neck cancer patients treated with concurrent chemoradiotherapy and preventive swallowing exercises. *European Archives of Oto-Rhino-Laryngology, **272**(11): 3521-31*.
16. Aghajanzadeh M, Ghorbani A, Torabinezhad F, Reza Keyhani M (2012) Comparing two Persian passages in laboratory evaluation of mean and fundamental frequency variations range. *Audiology, **21**(1): 62-68*.
17. Teixeira JP and Fernandes PO (2015) Acoustic analysis of vocal dysphonia. *Procedia Computer Science, **64**: 466-73*.
18. Moradi N, Pourshahbaz A, Soltani M, Javadipour S (2013) Cutoff point at voice handicap index used to screen voice disorders among persian speakers. *Journal of Voice, **27**(1): 130. e1-. e5*.
19. Aghadoost O, Moradi N, Dabirmoghaddam P, *et al.* (2016) Voice handicap index in Persian speakers with various severities of hearing loss. *Folia Phoniatrica et Logopaedica, **68**(5): 211-15*.
20. Bagherzadeh S, Shahbazi-Gahrouei D, Torabinezhad F, *et al.* (2022) The effects of (chemo) radiation therapy on the voice and quality of life in patients with non-laryngeal head and neck cancers: a subjective and objective assessment. *Int J Radiat Res, **20**(2): 397-402*.
21. Davies-Husband C, Murphy J, Kelly C, *et al.* (2018) Extreme long-term voice outcomes after concurrent chemoradiotherapy for advanced non-laryngeal head and neck cancer: Eight-year post-treatment analysis. *Clinical Otolaryngology, **43**(6): 1494-9*.
22. Paleri V, Carding P, Chatterjee S, *et al.* (2012) Voice outcomes after concurrent chemoradiotherapy for advanced nonlaryngeal head and neck cancer: a prospective study. *Head & Neck, **34**(12): 1747-52*.
23. Radhakrishna N, Yamini B, Kadam AS, *et al.* (2017) Acoustic analysis of voice in nonlaryngeal head and neck cancer patients post chemoradiotherapy. *J Cancer Research and Therapeutics, **13** (1):113-117*.
24. Sanguineti G, Adapala P, Endres EJ, Brack C, Fiorino C, Sormani MP, *et al.* (2007) Dosimetric predictors of laryngeal edema. *Int Journal of Radiat Oncolo Biolo Phys, **68**(3): 741-9*.
25. Agarwal JP, Baccher GK, Waghmare CM, Mallick I, Ghosh-Laskar S, Budrukkar A, *et al.* (2009) Factors affecting the quality of voice in the early glottic cancer treated with radiotherapy. *Radiotherapy and Oncology, **90**(2): 177-82*.
26. Lechien JR, Khalife M, Huet K, Fourneau A-F, Delvaux V, Piccaluga M, et al. (2018) Impact of chemoradiation after supra-or infrahyoid cancer on aerodynamic, subjective, and objective voice assessments: a multicenter prospective study. *Journal of Voice, **32** (2): 257. e11-. e19*.
27. Dehqan A, Yadegari F, Scherer RC, Dabirmoghadam P. (2017) Correlation of VHI-30 to acoustic measurements across three common voice disorders. *Journal of Voice, **31**(1): 34-40*.
28. Niebudek-Bogusz E, Woznicka E, Zamyslowska-Szmytke E, Sliwinska-Kowalska M. (2010) Correlation between acoustic parameters and Voice Handicap Index in dysphonic teachers. *Folia Phoniatrica et Logopaedica, **62**(1-2): 55-60*.
29. Wheeler KM, Collins SP, Sapienza CM (2006) The relationship between VHI scores and specific acoustic measures of mildly disordered voice production. *Journal of Voice, **20**(2): 308-17*.
30. Ziwei Y, Zheng P, Pin D (2014) Multiparameter voice assessment for voice disorder patients: a correlation analysis between objective and subjective parameters. *Journal of Voice, **28**(6): 770-4*.
31. Fujiki RB and Thibeault SL (2021) Examining relationships between GRBAS ratings and acoustic, aerodynamic and patient-reported voice measures in adults with voice disorders. *Journal of Voice, 1-7*.

[DOI: 10.52547/ijrr.21.2.7]