Voice Quality in Laryngeal Cancer Patients: A Randomized Controlled Study of the Effect of Voice Rehabilitation

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Abstract: Objectives. The study aimed to investigate the short-term and long-term effects of voice rehabilitation in patients treated with radiotherapy for laryngeal cancer as measured by both the acoustic measure smoothed cepstral peak prominence (CPPS) and perceptual measures. A secondary aim was to investigate the relationship between acoustic and perceptual measures.

Methods. In total, 37 patients received voice rehabilitation post-radiotherapy and 37 patients constituted the irradiated control group. Outcome measures were mean CPPS for connected speech and ratings with the auditory-perceptual Grade, Roughness, Breathiness, Asthenia and Strain (GRBAS) scale. Outcome measures were analyzed 1 (baseline), 6, 12, and 24 months post-radiotherapy, where voice rehabilitation was conducted between the first two time-points. Additional recordings were acquired from vocally healthy participants for comparison.

Results. CPPS values of the voice rehabilitation group and vocally healthy group were not significantly different at 24 months post-radiotherapy. Ten out of 19 patients who received voice rehabilitation yielded a CPPS value above the threshold for normal voice 24 months post-radiotherapy, compared to 11 out of 26 in the irradiated control group. No statistically significant correlations were found between CPPS and perceptual parameters of GRBAS.

Conclusion. Voice rehabilitation for irradiated laryngeal cancer patients may have positive effects on voice quality up to 24 months post-radiotherapy. The relationship between CPPS and GRBAS as well as the applicability of CPPS for evaluation over several points of measurement needs to be studied further.

Key Words: Laryngeal neoplasms−Voice therapy−Radiotherapy−Voice outcomes−Smoothed cepstral peak prominence.

INTRODUCTION

Laryngeal cancer accounts for 1.1 % of all cancer diagnoses, has an incidence of 157,000 new cases a year worldwide and is more common among men than women (7:1).[1] Radiotherapy is the main treatment for laryngeal cancer and while it provides good cure rates, patients often suffer from reduced voice function after the completion of treatment, including persistent roughness and increase in vocal fry.[2] Around 50% of patients have persisting voice problems for as long as 10 years post-radiotherapy.[3,4] Despite reported voice impairments post-radiotherapy and its risk of negative effects on the patients' quality of life,[5] evidence regarding the benefits of voice therapy in this population is scarce. Van Gogh et al.[4] investigated the effects of voice therapy for patients who experienced voice problems following radiotherapy or endoscopic laser surgery for early glottic tumors. The voice treatment provided did not follow a specified set of protocols regarding type of exercises, number of sessions, or timing in relation to oncologic treatment. Nevertheless, the treatment group improved significantly compared to the control group regarding self-assessed voice function, acoustic measurements jitter, noise-to-harmonics ratio, and the perceptual parameter vocal fry. A follow-up study revealed that the beneficial effects of voice therapy on acoustics and self-assessed voice function remained stable 1 year after the completion of voice therapy.[6]

To date, one randomized controlled group study investigating the effects of voice rehabilitation after radiotherapy treatment for laryngeal cancer has been published.[7−10] The follow-up was conducted with patient-reported measurements and health-related quality of life as well as acoustic and perceptual assessment up to 12 months following radiotherapy.[8−10] The voice rehabilitation, which followed a structured protocol, yielded a positive effect on patient-reported outcome measures. Although the acoustic analysis (jitter, shimmer, harmonics-to-noise ratio, and fundamental frequency) showed no significant differences between the intervention and control group, voice rehabilitation did appear to prevent a deterioration in the perceptual parameter roughness over time.

The perceptual parameter roughness has been described in a guideline for the European Laryngeal Society[11] as "audible impression of irregular glottic pulses, abnormal fluctuations in F0," thus resulting in an aperiodic audio signal. Cepstral peak prominence (CPP) and its smoothed measure, smoothed cepstral peak prominence (CPPS), have been suggested as more reliable measures for dysphonic voices than traditional perturbation measures, such as jitter and shimmer, which require some degree of periodicity in the audio signal to allow extraction of a fundamental frequency.[12,13] CPP is obtained from a cepstrum, which is a Fourier transform of a logarithm power spectrum of a voice

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signal. The cepstral peak prominence is a difference in amplitude, determined by the distance between the cepstral peak and the linear regression line below the peak. Averaging, or smoothing, the cepstrum across time and across quefrency by means of an algorithm for connected speech developed by Hillenbrand and Houde[14] extracts CPPS. A periodic audio signal has a higher degree of harmonicity in the spectrum, resulting in a more prominent peak than in an aperiodic signal, for example from a dysphonic voice. Analysis with CPPS can be performed on connected speech, which is an important advantage compared to the mentioned traditional perturbation measures. Clinical perceptual assessment of voice quality is often based on connected speech, where voice function in connected speech is of central value to the patient as it reflects communication in daily life. Maryn et al. concluded in a meta-analysis of acoustic measurements of overall voice quality that CPPS "can be regarded as the most promising and perhaps robust acoustic measure of dysphonia severity"[15] and in a recent meta-analysis CPPS was found to be one of the most robust acoustic measures to predict parameters roughness and breathiness.[16] A cut-off value for CPPS based on the Hillenbrand smoothing algorithm for CPP on samples of connected speech was established by Heman-Ackah et al. as 4.0 for normal voice quality, where values below 4.0 suggests presence of dysphonia.[17]

Current best practice is a multidimensional approach to voice evaluation,[11] and while many researchers have investigated the relationship between perceptual judgment and acoustic markers, the need to clarify this relationship further remains.[16] CPPS and CPP have previously been used as measures of voice changes over time in order to evaluate treatment effect for other patient groups.[18,19] Algorithms combining cepstral and spectral measures have been used for irradiated laryngeal cancer patients,[20] also in combination with GRBAS.[21]

The primary aim of the present study was to investigate the short-term and long-term effects of voice rehabilitation in patients treated with radiotherapy for laryngeal cancer as measured by both the acoustic measure CPPS and perceptual measures. A secondary aim was to investigate the relationship between CPPS and perceptual measures of GRBAS.

MATERIAL AND METHODS

Participants

All patients diagnosed with laryngeal cancer in the Västra Götaland region are presented on a weekly head and neck tumor conference where treatment options are discussed and decided for each patient. Between the years 2000 and 2011, with an interruption of 2 years, the patients who were to receive curatively intended radiotherapy ± chemotherapy were asked to participate in a study on voice rehabilitation. Inclusion criteria were sufficient cognitive ability and Swedish language competency to be able to fill in questionnaires independently and participate in voice rehabilitation sessions. Comorbidity was measured using the Adult Comorbidity Evaluation 27.[22]

Out of 194 patients assessed for eligibility, a total of 163 met the inclusion criteria and 89 of these chose to enroll in the randomized study and were allocated to voice rehabilitation group or irradiated control group. However, 12 patients discontinued their participation before the first follow-up, leaving a total of 77 patients. In the voice rehabilitation group, 37 patients were included for voice analysis. Out of the 40 patients constituting the irradiated control group, three patients were excluded due to voice recordings either missed (n = 2) or with poor sound quality (n = 1) at baseline, leaving 37 patients for voice analysis. A description of inclusion, exclusion, and discontinuation of patients is shown in a flowchart in Figure 1. No statistically significant differences between the voice rehabilitation group and the irradiated control group were found when patient clinical characteristics (gender, age, smoking status, tumor size and location, comorbidity, and type of oncological treatment) at baseline were compared, as shown in Table 1.

From baseline to 24 months, 18 patients from the voice rehabilitation group and 11 from the irradiated control group were lost to follow-up. Reasons were missed recording (n = 3), laryngectomy (n = 4), tracheostoma (n = 2), poor health (n = 9), and patient choice/no reason stated (n = 11). Drop-out analysis of the patients who discontinued (n = 29) compared to those who remained in the study (n = 45) showed no statistically significant differences regarding any of the aforementioned patient clinical characteristics.

Study design

This study builds on a recent randomized controlled study investigating the effects of voice rehabilitation after radiotherapy for laryngeal cancer by Karlsson et al.[9] and Bergstrom et al.,[8] with longer follow-up intervals. The computerized randomization procedure followed Pocock's sequential randomization method[23] for optimal allocation regarding age, gender, smoking habits, tumor site, tumor size and patients' self-evaluation of communication.[24] Sample size was determined by an 80% power calculation, with dysphonia as the main variable. The participants were randomized into groups of equal size, either intervention group or irradiated control group, where the intervention group received voice rehabilitation after completion of radiotherapy while the irradiated control group received general advice on vocal hygiene. Both groups were followed up with audio recordings and questionnaires at similar timepoints. The recordings were made at 1 (baseline), 6, 12, and 24 months post-radiotherapy.

Additional voice recordings were acquired from a group of volunteers without voice complaints (n = 25), matched on group level to the included patients regarding gender and age (mean age = 63 years). Volunteers were recruited from family of patients and hospital staff during 2013 and

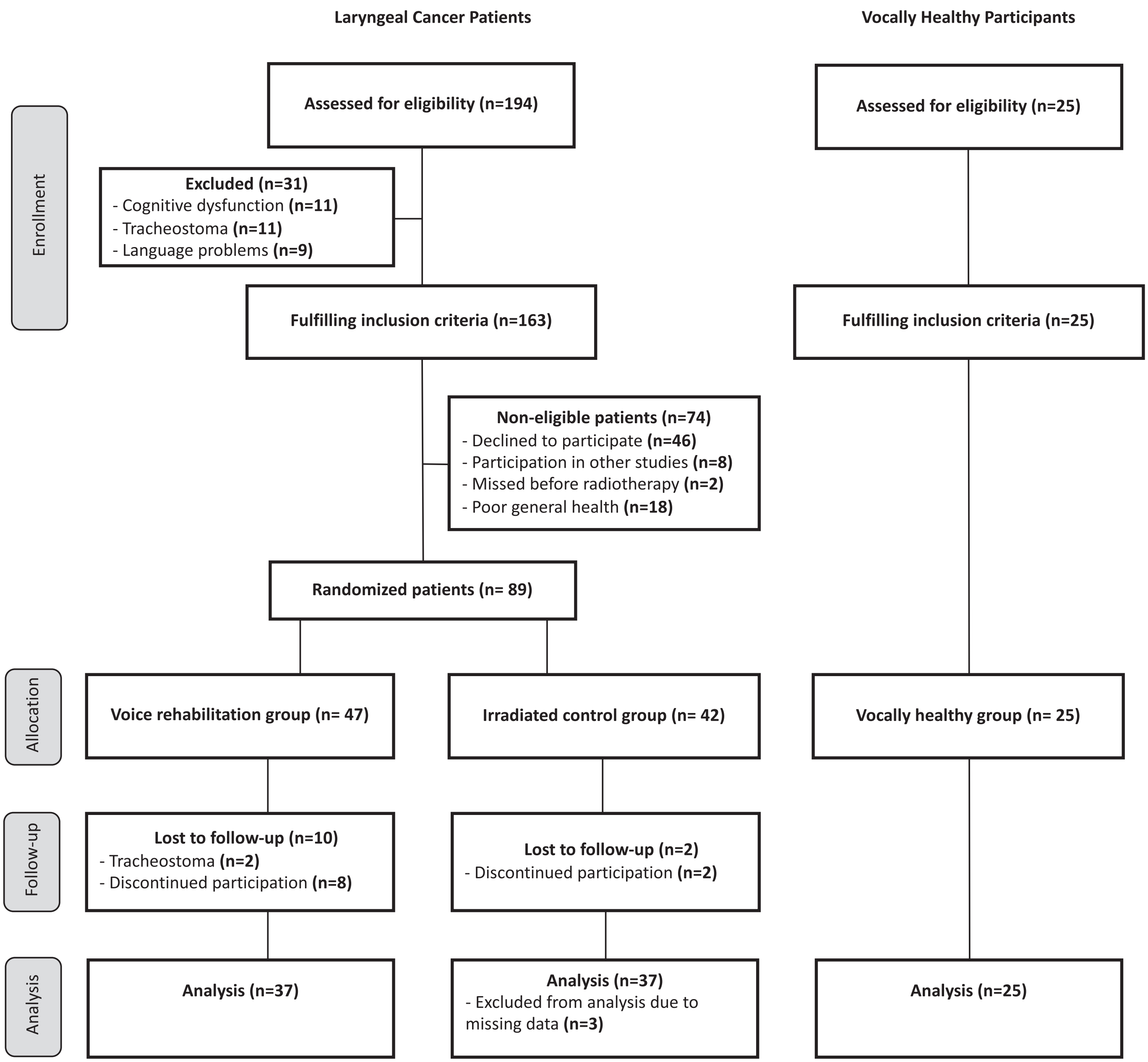

FIGURE 1. Description of inclusion, exclusion, and discontinuation of participants in the voice rehabilitation group, the irradiated control group, and the vocally healthy group.

were all assessed by an otorhinolaryngologist to confirm absence of vocal pathology.

Intervention

The voice rehabilitation was given by speech-language pathologists (SLPs) between 1 and 6 months post-radiotherapy. It consisted of 10 occasions over the course of 10 weeks, with approximately 30 minutes per treatment session. Each session included a prespecified set of breathing, relaxation and phonation exercises, and direct and indirect therapy techniques. The participants were asked to do voice exercises at home between sessions. The voice rehabilitation protocol has been described in detail elsewhere.[7]

Voice recordings

Voice recordings included reading a standard passage aloud and the maximum sustained vowel /a/ repeated three times. Recordings were made in a sound treated room at a sampling frequency of 44.1 kHz with a Panasonic Professional Digital Audio Tape Recorder SV-3800, using a head worn microphone (Sennheiser MKE 2-p) placed at a distance of 12 cm from the corner of the participant's mouth. All recordings were transferred from Digital Audio Tape to a

TABLE 1.
Clinical Characteristics and Comparisons Between the Voice Rehabilitation Group and the Irradiated Control Group at Baseline. Clinical Characteristics of the Vocally Healthy Group

	Voice Rehabilitation Group n = 37	Irradiated Control Group n = 37	Vocally Healthy Group n = 25
Age in years			
Mean (SD)	65.2 (12.3)	62.9 (10.0)	63.0 (9.4)
Median (range)	65.0 (35–86)	64.0 (41–82)	60.0 (46–84)
	n (%)	n (%)	n (%)
Gender			
Male	33 (89.2%)	33 (89.2%)	23 (92.0%)
Female	4 (10.8%)	4 (10.8%)	2 (8.0%)
Smoking status			
Non-smoker	6 (16.2%)	2 (5.4%)	10 (40.0%) *
Smoker	15 (40.5%)	19 (51.4%)	9 (36.0%) *
Quit smoking > 12 months prior to study	16 (43.2%)	16 (43.2%)	6 (24.0%) *
Comorbidity according to the ACE-27			
No comorbidity	14 (37.8%)	16 (43.2%)	n/a
Mild comorbidity	13 (35.1%)	15 (40.5%)	n/a
Moderate comorbidity	10 (27.0%)	6 (16.2%)	n/a
Severe comorbidity	0 (0.0%)	0 (0.0%)	n/a
Tumor location			
Supraglottic	6 (16.2%)	7 (18.9%)	n/a
Glottic	31 (83.8%)	29 (78.4%)	n/a
Subglottic	0 (0.0%)	1 (2.7%)	n/a
Tumor stage			
0	0 (0.0%)	2 (5.4%)	n/a
I	25 (67.6%)	19 (51.4%)	n/a
II	10 (27.0%)	11 (29.7%)	n/a
III	1 (2.7%)	5 (13.5%)	n/a
IV	1 (2.7%)	0 (0.0%)	n/a
Radiotherapy			
Conventional	27 (73.0%)	26 (70.3%)	n/a
Hyper-fractionated	10 (27.0%)	11 (29.7%)	n/a

Abbreviation: ACE, adult comorbidity evaluation 27.
Notes: There were no significant differences between the voice rehabilitation group and the irradiated control group.
* , statistically significant difference, $P < 0.05$, for the vocally healthy group regarding smoking status when compared to the voice rehabilitation group and the irradiated control group.

computer hard drive as digital audio files (.wav) by means of the software Swell Soundfile Editor, version 4.5 (Electronix Hitech).

Voice recordings were edited by means of the Swell Soundfile Editor to obtain only the first two sentences of the standard passage for acoustic analysis and perceptual assessment, with the addition of the second recorded prolonged vowel /a/ for perceptual assessment.

Acoustic analysis

The CPPS for connected speech was calculated using the SpeechTool software (James Hillenbrand, Western Michigan University, https://homepages.wmich.edu/~hillenbr/, last inspected November 9, 2017). Prior to analysis, all voice samples were downsampled to 22.05 kHz because of software requirements.

Perceptual assessment

Perceptual ratings were conducted by two SLPs who had not been involved in the treatment of any of the participants, blinded to patient status and voice sample information. Where the two raters disagreed on a sample, a third SLP provided an additional rating so that agreement between two out of three raters was reached and used as the final rating for analysis. The assessment protocol was the GRBAS scale,[25] consisting of grade, roughness, breathiness, asthenia, and strain. Grade represents the overall impression of voice quality impairment and is rated based on the highest rated value of any of the other four parameters. Each voice quality parameter is rated on a 4-point scale, where 0 = normal, 1 = mildly impaired, 2 = moderately impaired and 3 = severely impaired. In addition to GRBAS, raters were also asked to rate presence of vocal fry on a 4-point scale. Raters attended a half-day's consensus training and were provided with reference voice samples representing each of the voice quality parameters in the GRBAS protocol and vocal fry. Reference voice samples were to be listened to for every 20th voice sample rated. Furthermore, 20% of the voice samples were randomized duplications for intrarater reliability purposes.

Statistical analysis

All analyses were performed using Statistical Package for the Social Sciences (SPSS, IBM, Sweden) version 24 for Mac and Microsoft Excel for Mac, version 16.10. Nonparametric tests were used due to the non-normal distribution of the data. All tests were two-tailed with the level of significance set to $P < 0.05$ throughout.

For descriptive purposes mean, standard deviation, median and range were extracted. To explore differences in baseline characteristics between groups, Fisher's exact test was used for dichotomous variables, Mantel-Haenszel Chi-square test for ordered categorical variables, Chi-square test for nonordered categorical variables and the Mann-Whitney U-test for continuous variables. Paired analyses of changes over time within groups were done with Wilcoxon Signed Rank test for continuous variables and Sign test for ordered categorical variables. For between group comparisons, the Mann-Whitney U-test and Mantel-Haenszel Chi-square exact test were used. The Spearman correlation coefficient was used to measure the strength of association between acoustic and perceptual variables. Inter- and intrarater reliabilities were calculated using percent exact agreement and Weighted Kappa.

Ethical considerations

This study was conducted in accordance with the Declaration of Helsinki with the approval of the Regional Ethical Review Board in Gothenburg, Sweden. All participants gave their informed consent before inclusion in the study.

RESULTS

Acoustic data

Effect of voice rehabilitation on the acoustic measure CPPS is presented in Table 2. There were no statistically significant differences between the voice rehabilitation group and irradiated control group regarding CPPS at any study occasion. Comparisons between CPPS of the irradiated control group at all study occasions with those of the vocally healthy group yielded statistically significant differences. CPPS values for the voice rehabilitation group also differed significantly from those of the vocally healthy group at baseline, 6 and 12 months follow-up. However, at the 24-months follow-up, there was no longer a statistically significant difference in value of CPPS for the voice rehabilitation group compared to the value of CPPS for the vocally healthy group. Furthermore, the median value of CPPS at the 24-months follow-up was 4.03 for the voice rehabilitation group, reflecting the fact that 10 out of 19 patients (52.6%) in this group reached a value above the threshold for what is considered a normal voice ($\geq$4.0),[17] at the final study occasion. Corresponding values for the irradiated control group at 24 months were 11 out of 26 patients (42.3%) with CPPS $\geq$ 4.0 and a median value of 3.56.

Perceptual data

The perceptual parameter asthenia showed only a mild degree in less than five patients at all study occasions and was excluded from further analysis because it would not provide any discrimination about overall voice quality. There were no statistically significant differences between the groups in any perceptual parameter at baseline.

Comparisons between groups

Statistically significant differences between the voice rehabilitation group and the irradiated control group were found at two study occasions only. At 6 months, the voice rehabilitation group showed statistically significant inferior values of breathiness compared to irradiated controls (P = 0.049) and at 12 months (P = 0.013) the irradiated control group presented with statistically significant inferior values of roughness compared to the voice rehabilitation group. At 24 months the irradiated control group was rated as statistically significantly worse on all perceptual parameters compared with values of the vocally healthy group, whereas the voice rehabilitation group and the vocally healthy group did not differ significantly on the parameters breathiness and vocal fry, indicating an improvement in the voice rehabilitation group.

Comparisons within groups

A statistically significant improvement in breathiness (P = 0.012) occurred between 12 and 24 months follow-up for the voice rehabilitation group. There was a statistically significant deterioration of vocal fry within each group respectively. A total of 3 (8.1%) patients in the irradiated control group presented with moderate-severe vocal fry at baseline and at the 24 months follow-up, this figure was 11 out of 26 patients (44%, P = 0.003). However, at 6 months 2 out of 35 patients (5.7%) in the voice rehabilitation group were rated with moderate-severe vocal fry and at 24 months, this figure was 4 out of 19 patients (21.1%, P = 0.012). The irradiated control group also demonstrated a statistically significant deterioration of roughness from 6 to 12 months follow-up (P = 0.027), which has been previously reported elsewhere.[26] Comparisons within groups are displayed in Figure 2.

Comparisons of changes between groups

Changes in vocal quality over time within groups compared between the voice rehabilitation group and the irradiated control group were divided into the categories “improvement,” “deterioration,” and “no change.” Only the patients with recordings from both of the study-points compared

TABLE 2.
Acoustic Analysis at Baseline (Before Start of Voice Rehabilitation) and at 6, 12, and 24 Months Follow-Up of the Voice Rehabilitation Group and the Irradiated Control Group, and Acoustic Analysis of the Vocally Healthy Group

	Voice Rehabilitation Group				Irradiated Control Group				Vocally healthy group
	Baseline (1 m post RT) n = 37	6 months post RT n = 35	12 months post RT n = 31	24 months post RT n = 19	Baseline (1 m post RT) n = 37	6 months post RT n = 35	12 months post RT n = 33	24 months post RT n = 26	n = 25
	Mean (SD) Median (min-max)	Mean (SD) Median (min-max)	Mean (SD) Median (min-max)	Mean (SD) Median (min-max)	Mean (SD) Median (min-max)	Mean (SD) Median (min-max)	Mean (SD) Median (min-max)	Mean (SD) Median (min-max)	Mean (SD) Median (min-max)
Mean CPPS	3.53 (1.06) 3.55 (1.23-5.86)*	3.52 (0.90) 3.57 (1.56-5.34)*	3.48 (1.11) 3.79 (1.20-5.42)*	3.79 (0.90) 4.03 (2.04-5.26)	3.25 (1.00) 3.42 (1.38-5.02)*	3.24 (0.99) 3.29 (1.28-5.30)*	3.44 (1.04) 3.73 (1.62-5.10)*	3.52 (1.18) 3.56 (1.43-5.63)*	4.27 (0.68) 4.27 (2.82-5.40)
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
No. of patients above threshold for CPPS ≥ 4.0	15 (40.5%)	13 (37.1%)	10 (32.3%)	10 (52.6%)	10 (27.0%)	10 (28.6%)	11 (33.3%)	11 (42.3%)	16 (64%)

Abbreviations: CPPS, smoothed cepstral peak prominence; RT, radiotherapy.
Notes * ,Statistically significant difference compared to values of the vocally healthy group $P < 0.05$. There were no statistically significant different values of CPPS between the voice rehabilitation group and the irradiated control group at any study occasion. A value of mean CPPS below 4.0 indicates a dysphonic voice.

were included in the analysis. The number of patients with recordings per follow-up is shown in Table 2. Comparisons revealed a statistically significant difference between groups regarding the changes for vocal fry from baseline to 6 months (P = 0.046). Out of a total of 35 patients in the voice rehabilitation group, 11 (31.4%) improved and 7 (19.7%) deteriorated. Corresponding values for the irradiated control group were 5 patients (14.3%) who improved and 13 patients (37.2%) who deteriorated, out of a total of 35 patients. Changes of breathiness were statistically significant between groups from baseline to 6 months (P = 0.041) and from 12 to 24 months (P = 0.022). In the voice rehabilitation group 7 out of 35 patients (20%) showed improvement and 15 out of 35 patients (42.8%) deteriorated from baseline to 6 months, while 15 out of 35 patients (42.9%) in the irradiated control group showed improvement and 9 out of 35 patients (25.7%) deteriorated. From 12 to 24 months the findings were reversed, where 10 out of 19 patients (52.6%) in the voice rehabilitation group improved and 1 out of 19 patients (5.3%) deteriorated compared to the irradiated control group, in which 8 out of 26 patients (30.8%) showed improvement and 10 patients out of 26 patients (38.4%) showed deterioration.

Reliability of perceptual ratings

Inter- and intrarater reliabilities were calculated for the two raters using percent exact agreement (PEA) and Weighted Kappa. Inter-rater reliability revealed a PEA of 53.6%. Weighted Kappa was calculated at 0.41, indicating a moderate agreement.[27] Intrarater reliability revealed PEA 77.8% and a Weighted Kappa of 0.77 (indicating a substantial agreement) and PEA 61.90% and a Weighted Kappa of 0.55 (indicating a moderate agreement) for the raters respectively.

Correlations

Analysis of CPPS and parameters of GRBAS at all study occasions for all patients revealed no statistically significant correlations.

DISCUSSION

This study is, to the authors' knowledge, the first to investigate the effect of voice rehabilitation in patients treated with radiotherapy for laryngeal cancer by means of CPPS in a randomized controlled trial. The CPPS was hypothesized to be a suitable measure of roughness and irregularity in the voices of patients treated with radiotherapy. Outcome measures of the effect of voice rehabilitation were the acoustic measure CPPS, ratings with the auditory-perceptual GRBAS scale, and rated degree of vocal fry up to 24 months post-radiotherapy.

Voice rehabilitation has shown positive effects on patient-reported outcomes for irradiated laryngeal cancer patients and also prevents deterioration of roughness,[8–10] but more studies are needed on this subject. These should preferably be randomized trials with long-term follow-ups and the present study is an attempt to explore such long-term effects further. The guidelines of the European Laryngeal Society[11] emphasize the multidimensional approach for evaluation of voice, with acoustics being one of these dimensions. While perturbation and noise measures have been suggested to be less suitable as a measure of severely dysphonic voices, CPPS has been highlighted as a possible tool since it can be applied to connected speech and is not sensitive to unvoiced segments.[13,28] Furthermore, in the present study, the GRBAS was rated on connected speech and there was a need to investigate if these ratings correlated with the acoustic measures of the same material, i.e. the connected speech and not just an isolated vowel.

Results revealed that patients who received voice rehabilitation were not significantly different on measures of CPPS, breathiness and vocal fry at 24 months follow-up when compared to a group of vocally healthy participants. These results indicate that after 2 years, the voice rehabilitation group became more comparable to the vocally healthy group in these parameters. Furthermore, the median value of CPPS for the voice rehabilitation group was ≥ 4.0 at 24 months and 10 out of 19 patients were at, or above, the threshold for normal voice quality.[17] The change in breathiness in the voice rehabilitation group between 12 and 24 months, significantly different from the irradiated control group, is an interesting feature. Watson et al.[29] found that the voice quality of laryngeal cancer patients remained relatively stable from 12 months to 10 years post-radiotherapy but did not reach values comparable to those of a "normal" population on parameters breathiness, roughness, strain, and vocal fry. The changes of breathiness and difference between groups in the present study may be attributed to the voice rehabilitation and studies of voice outcomes more than 2 years post-radiotherapy could further clarify any long-term effects of voice rehabilitation. The absence of correlation between CPPS and perceptual parameters differed from previous studies, where CPPS has shown correlation with breathiness and roughness.[16] In previous studies, CPPS has mostly been used to distinguish dysphonic voice from normal voice, while in the present study most patients remained dysphonic throughout the study, albeit with varying degrees. It is clear that CPPS as a measure of voice change over time within a dysphonic population needs further investigation. It is also worth emphasizing the importance of high-quality audio recordings at follow-up for successful analysis, both perceptual and acoustic.

The vocally healthy group had CPPS values that might be expected to be higher, i.e. better, with only 64% presenting with voices above the threshold 4.0. Over a third of the vocally healthy participants were smokers and might be likely to have more hoarse voices than nonsmokers. Verdonck-de Leeuw and Mathieu concluded in a study of healthy men that aging of the voice led to a deterioration of roughness and that smokers did develop more creaky voices compared to nonsmokers.[30] Creaky voice is another term for vocal fry.[31] Heman-Ackah et al.[17] presented the cut-off

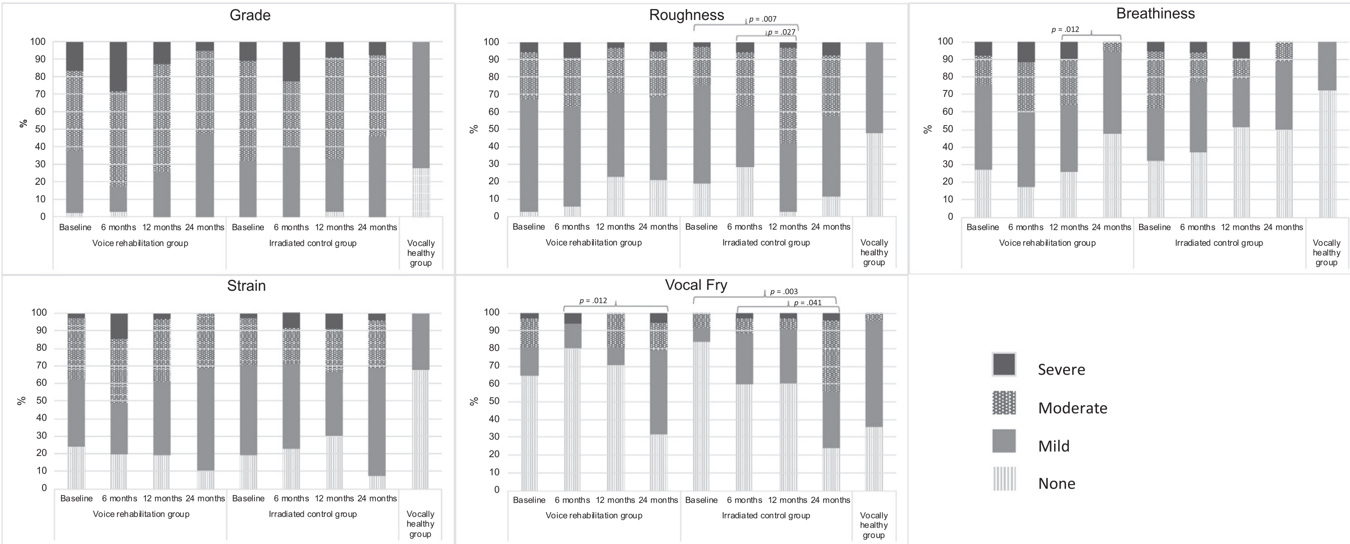

FIGURE 2. Ratings of voice quality for the voice rehabilitation group and the irradiated control group at all four study occasions. Ratings of voice quality for the vocally healthy group. Statistically significant changes within group are presented with brackets.

value of CPPS as being ≥ 4.0 for normal voices, albeit no information was given about the age of the participants in their study. What should be considered a "normal" value of CPPS when taking typical age-related vocal changes into account could certainly be a topic for further investigation when it comes to a population of a mean age over 60, like the participants in the present study.

The significant difference in change of the parameter breathiness between the voice rehabilitation group following voice therapy and the irradiated control group at the 6 months follow-up indicates that patients who received voice therapy got more breathy voices. During the same time period the voice rehabilitation group improved significantly regarding vocal fry compared to the irradiated control group. Bergstrom et al.[8] suggested that the use of easy-onset and breathy-voice techniques may have influenced the degree of perceived breathiness in the voice rehabilitation group. In a study of efficacy of voice therapy in patients with vocal nodules, Holmberg et al. concluded that although most patients in their study increased in breathiness following voice therapy, breathiness alone should not be used as a measure of efficacy, but rather considered in relation to press, and the increase in breathiness may reflect decreased hyperfunction of phonation and improved voice function.[32] In addition, Hammarberg et al.[31] proposed a bipolar relationship between breathy voice quality and vocal fry/creaky voice (also described as "overtightness"). The pattern of increase/decrease of breathiness and vocal fry of the voice rehabilitation group in the present study suggests a similar tendency. Moreover, it can be speculated that vocal fry is a relatively easy parameter for both the SLP and the patient to monitor, thus leading to a decrease of presence of vocal fry during voice rehabilitation but that deterioration happens again after some time, unless the patient actively maintains the vocal techniques achieved over the sessions.

The protocol for the voice therapy given in this study was a combination of direct and indirect voice therapy techniques, which is in accordance with evidence for functional dysphonia.[33] However, the best available treatment options for the irradiated population needs to be further explored, since the underlying causes of their voice problems are different from patients' with primarily functional dysphonia. Effects of radiotherapy have been reported as scarring of the vocal folds, inflammation, edema, fibrosis, impaired vocal fold function such as incomplete glottal closure and limited mobility[34,35] and xerostomia (hypofunction of salivary glands), which has been shown to contribute to poor vocal function.[36] Karlsson et al. suggested that voice rehabilitation for irradiated patients should target roughness, breathiness and strain and recommended early intervention to prevent the risk of developing adverse compensatory vocal behaviors.[26] For future studies on voice rehabilitation it might be worth to explore focusing on semi-occlusion exercises[37] and the use of resonance tube in water for its suggested effects on laryngeal relaxation and modulation of vocal fold movements.[38,39] The problem with dryness of mouth and throat and its effect on voice function was addressed by Tanner et al. in a study on patients with Sjögrens syndrome treated with nebulized saline, which found that the re-hydration had positive effects on patient-reported measurements and voice acoustics.[40] The influence of xerostomia on voice rehabilitation for irradiated patients could be explored further. For future studies it might also be advantageous to develop a protocol for voice rehabilitation specified not only for sessions, but also for the patients' independent exercises in between sessions. This could be done by giving patients instructions on duration and frequency of the voice exercises and also to record themselves during their sessions at home for the SLP to spot-check, as has been done in previous studies.[32] This could facilitate evaluation of compliance and also allow the SLP to further follow the patients' progress and customize the exercises when needed.

There were limitations in this study, namely that a considerable number of patients were lost to follow-up at the final study occasion. This was particularly notable in the voice rehabilitation group, which decreased in size to about two-thirds of the patients from the 12 months follow-up. There was no set protocol for how the patients were to do the voice exercises at home, hence it was not possible to assess their compliance to the voice rehabilitation. The inter-rater agreement of the GRBAS was moderate, which needs to be taken into consideration when interpreting the results. It would have been ideal to explore the correlations between CPPS and the GRBAS parameters further, with a larger number of expert raters, despite the big material posing a challenge.

In the present study, CPPS was used as an outcome measure of the effect of voice rehabilitation for irradiated voices and this study is one of the very few where CPPS has been used to evaluate voice changes over time. It is also, to the authors' knowledge, the first time CPPS has been used in a study with Swedish speakers, which calls for further studies of CPPS for this population. A full multimodal evaluation including patient-reported outcomes and laryngeal examination in accordance with the guidelines from European Laryngeal Society would have been advantageous and should be considered for future studies.

CONCLUSIONS

CPPS values, degree of breathiness, and degree of vocal fry of the voice rehabilitation group were not significantly different from a vocally healthy group at 24 months post-radiotherapy, indicating that voice rehabilitation for irradiated laryngeal cancer patients may have positive effects on voice quality over a period of up to one and a half years after completion. Ten out of 19 patients who received voice rehabilitation yielded a CPPS value above the threshold for normal voice 24 months post-radiotherapy, compared to 11 out of 26 in the irradiated control group. The relationship between CPPS and GRBAS, as well as the applicability of CPPS for evaluation over several points of measurement, needs to be studied further.

DECLARATION OF INTERESTS

None to declare.

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