

The Relationship between a Patient and Clinician Reported Voice Tool in Pharyngeal and Laryngeal Cancer Post Organ Preservation

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ABSTRACT

Background: Patients with pharyngeal and laryngeal cancers have voice problems either secondary to the tumour, treatment or both.

Aim: To study the relationship between a patient and a clinician reported voice tool in pharyngeal and laryngeal cancer undergoing organ preservation.

Methodology: This was a prospective, cohort study conducted over 2 years at a single tertiary care center. The relationships between the voice handicap index (VHI) and GRBAS scale were studied in pharyngeal and laryngeal cancers before and after organ preservation. Mann Whitney U and Spearman's correlation were used for the statistical analysis.

Results: Twenty-two patients (eighteen men and four women) were studied. In the pharyngeal group, before treatment, only 'roughness' component of GRBAS had strong positive correlations with VHI domains and total VHI scores ($P < .05$, $r = > .60$). However, after treatment most parameters of GRBAS and VHI were strongly correlated ($P < .05$, $r = > .60$). In the laryngeal group strong correlations were found between all the parameters of GRBAS and VHI both before and after treatment. All VHI and GRBAS scores were significantly different ($P < .05$) between the pharyngeal and laryngeal cohort before treatment, while after treatment only roughness, breathiness, asthenia, and strain were significantly different.

Conclusion: VHI and GRBAS are two common tools used for voice assessment. In laryngeal cancer even a small complaint should be treated with high index of suspicion indicating a thorough evaluation (strong positive correlation). However, in pharyngeal cancer any gross change in voice should be evaluated (positive correlation).

Keywords: Voice handicap index, GRBAS, Pharyngeal cancer, Laryngeal cancer, Organ preservation, Chemoradiation

INTRODUCTION

Voice changes in laryngeal and pharyngeal cancers may be due to neuromuscular paresis of the vocal cord affecting its mobility, obstruction of glottic airflow, post-radiation fibrosis, edema or atrophy of the surrounding tissues. ^[1,2]

Assessment of voice is one of the important aspects in clinical examination of head and neck patients. These patients can present with self-reported voice change or are incidentally noticed to have voice change by clinicians, family members or others. There are various tools to assess voice changes among which are two

common tools namely the VHI (voice handicap index) and GRBAS (Grade, Roughness, Breathiness, Asthenia, Strain). VHI is a self-reported tool whereas GRBAS scale is a clinician reported tool which has been used to study patients' perceptions on voice change and voice quality post chemoradiation in pharyngeal and laryngeal cancers. [1,3-10]

There are a few studies which have analysed the correlations between voice related quality of life measures with other clinical voice assessment tools. [11-12] Since both VHI and GRBAS are subjective tools the relationships between them were of concern. The patient's perception of their voice change can defer from that of a clinician. Hence there may be disparity between VHI and GRBAS outcomes. Therefore, there is a need to study the relationships between VHI and GRBAS for patients with laryngeal and pharyngeal cancers before and after chemoradiation. The aim of the current study was to understand the relationship between a patient and a clinician reported voice tool in pharyngeal and laryngeal cancer undergoing organ preservation.

METHOD

This was a prospective single tertiary care centre cohort study conducted over a period of two years. The study was approved by the institutional review board and ethics committee of the institutions participating in the study {Ref: NH/IRB-CL-2 014-170-(4-6-2014) and NHH/MEC-CL-2014/230-(5.7.2014)}. Patients enrolled into this study were those with biopsy proven T1-T4 pharyngeal and laryngeal cancers, who presented to the department of head and neck oncology, and were chosen for organ preservation treatment based on the National Cancer Comprehensive Network guidelines decided at a multidisciplinary tumour board meeting. [13] The patients with carcinomas of the oropharynx and hypopharynx and all subsites of the larynx were included. Those with tracheostomy and feeding tubes were included while those

with a history of pre-existing neurological disorders, nasopharyngeal carcinoma, surgeries to the primary tumor site were excluded from the study. Therefore, a total of twenty-two patients of which eighteen males and four females were enrolled into the study.

The main modality of treatment was organ preservation which included both radiotherapy (RT) and chemotherapy (CT). The total dose delivered to the primary tumour and involved lymph nodes were 70 Gy (two Gy per fraction, one fraction per day, five fractions per week). The dose to the spinal cord was kept below 46 Gy. This was combined with weekly cisplatin 40 mg/m² in six weekly cycles starting on the first day of radiation depending on the protocol.

Assessment

Voice assessment was carried out 2-3 days before the initiation of treatment and 3-9 months after treatment. The assessment included the use of VHI which is a self-administered perception tool and GRBAS, a clinician administered tool.

Voice handicap index (VHI)

The VHI is a self-reported quality of life measure. [14] It incorporates various questions which measure the patients perceived consequences of the vocal fold pathology. It assesses the impact of the voice disorder on three main domains mainly (E) emotional, (P) physical and (F) functional aspects of their lives. It is a 5-point rating scale varying from *score* (0) which indicated that the patient never experienced such a phenomenon to *score* 4 which meant they always had these experiences. Scores in each domain (emotional, physical, and functional) ranged from *score* (10) which meant they were (unaffected) to *score* (40) which meant that they were (severely affected), thus the total *score* (T) summed up all the three domains. Based on the scores obtained, they were categorized into four groups - No complaints (*score* 0), mild voice handicap

(score 1-30), moderate voice handicap (score 31-60) and severe voice handicap (score 61-120).

GRBAS

To measure the quality of voice clinicians used the GRBAS rating scale which was developed by the Japanese Society of Logopedics and Phoniatrics. [15] The parameters measured were 'grade' which described the overall degree of hoarseness, 'roughness' which denoted the auditory and acoustic impression of irregularity of vibration like jitter and shimmer. 'Breathiness' denoted the degree of air leakage related to the turbulence, 'asthenia' which was related to the weakness or lack of power related to vocal intensity and energy in the higher harmonics. 'Strain' denoted the auditory and acoustic impression of hyperfunction related to fundamental frequency, noise in high frequency range and energy in the higher harmonics. It is a 4-point rating scale ranging from score (0) to score (3), where score (0) is normal and score (3) is extreme. Thus, the GRBAS score summed up all the five domains.

Procedure

Before the initiation of data collection, informed consent was taken from all the patients. They were oriented about the study design and were instructed to fill up the questionnaire after reading the questions and statements from the VHI tool and scoring them according to their perceived problems. If they were unable to read, the investigator read out the questions and gave them appropriate examples till they understood.

The second task involved a voice recording of a narrative of the thirsty crow story which was commonly known. Nine black and white pictures of A4 size each were placed in a serial order in a file. After a preparatory time of 1 minute they were encouraged to describe the pictures for at least 2 minutes. To carry out the speech recordings a Toshiba laptop, Logitech H

340 USB computer headset with attached noise cancelling digital microphone was used. It had an input impedance of 20 ohms, a headphone sensitivity of 115 dB \pm 3 dB with a frequency response between 20Hz-20kHz. It also had a microphone sensitivity of -42dBV/Pa \pm 3dB with a frequency response between 100Hz- 16 kHz. The cable length was 1.8m and it was USB compatible (1.1, 2.0, 3.0). PRAAT software version 5.4 was used to record the speech stimuli. The recording levels were monitored on the VU meter. A constant mouth to microphone distance of ~ 12 cm was maintained for all the patients.

Data Analysis

The patient scores were collated and calculated for each domain of VHI. A sum of all the three domains provided the overall severity of voice handicap. For the second task the primary investigator who had more than 10 years of experience in head and neck oncology played back the narrative of the thirsty crow story as an offline experiment in a quiet room. The intensity of each audio file was averaged to 70 dB which was comfortable to comprehend spoken utterances. The audio files were played back through PRAAT connected to an external speaker (Creative A 235 Model No MF0400) and GRBAS was scored both before and after treatment.

Statistics

Data was collected and stored in a hard drive. Once the results were calculated they were transferred to an excel sheet and were in turn analysed using IBM SPSS® version 26. Mann Whitney U test was used to study the differences and Spearman's correlation method was used to study the relationships between the two groups. The level of alpha in this study was taken as 0.05. The estimate of the Pearson product moment correlation coefficient was denoted by r . r values which ranged from .80 to 1.00 (-.80 to -1.00) were considered a very strong positive or very strong negative correlation. The r value range of .60 – .79 (-.60 to -.79)

were considered a strong positive or strong negative correlation. No correlation was denoted by a coefficient of 0. As the characteristics of the cohort population were different, data of both VHI and GRBAS were analysed separately for pharyngeal and laryngeal cancers.

RESULTS

Demographic history

There were twenty-two patients enrolled into the study of which twelve patients had carcinoma of the pharynx and ten patient's carcinomas of the larynx. In the pharyngeal group, there were a total of nine males and three females with a mean age of 58.50 ± 9.17 years. Of them, one had a T0 tumour, one had a T1 tumour, five had T2 tumours, three had T3 tumours and two had T4 stage of tumours. Out of them two had N0 nodes, four had N1 nodes, five had N2 nodes and one had N3 nodes. Two patients could not be evaluated for metastasis and the remaining ten patients had no metastasis detected. Out of the twelve patients, six patients had tumours in the hypopharynx and six in the oropharynx. Of the six patients who had tumours in the hypopharynx, one patient had a tumour in the post cricoid region and five had tumours in the pyriform sinus. Among the six oropharyngeal tumours, one had a tumour in the soft palate, two patients had tumours in the base of tongue, two in the tonsil and one in the lateral pharyngeal wall. All patients underwent CRT, one with neo-adjuvant chemoradiation and the other with neck dissection preceding organ preservation treatment. Ten patients underwent intensity-modulated radiation therapy (IMRT) and two patients underwent 3D conformal radiation therapy (3DCRT).

Out of the ten patients diagnosed with laryngeal cancer nine were males and one female with a mean age and standard deviation of 53.70 ± 11.31 years. Of these, three had stage I, one stage II and six stage III tumours. Six had N0 nodes and four had N2 nodes. No metastasis was detected in seven patients while in three a full workup

for metastases could not be done. Among the ten patients, five had supraglottic tumours, four had glottic tumours and one had a subglottic tumour. Three patients received primary radiation only, and seven underwent chemoradiation. Seven patients were treated with intensity modulated radiation therapy (IMRT), one with three-dimensional conformal radiation therapy (3DCRT) and two patients with image guided radiation therapy (IGRT). In both groups, patients undergoing both treatments and their techniques were analyzed together. Two patients had tracheostomy tubes before treatment and they remained even after treatment. The results of the study are described below using the following variables.

Correlation between GRBAS and VHI Pharyngeal Cancer

The correlation of VHI and GRBAS in patients with pharyngeal cancer pre-treatment and post-treatment using Spearman's correlation method is depicted in (table 1). The overall correlation between VHI and GRBAS was weak before treatment. The 'roughness' component of GRBAS had a strong positive correlation with the functional and physical domains of VHI along with the total VHI score ($P < .05$, $r = .60$ to $.79$). Similarly, the total GRBAS score was also strongly correlated to the emotional domain ($P = .02$, $r = .67$). A very strong positive correlation existed between 'roughness' and the emotional domain ($P = .00$, $r = 1.00$).

However, the stronger relationships between variables increased post-treatment. Except asthenia all the other parameters of GRBAS, including the total score had a strong positive correlation with VHI ($P < .05$, $r = .60$ to $.79$). Grade had a strong positive correlation with the functional, physical, and emotional domains including the total VHI scores and overall severity category. Roughness also had a strong positive correlation with the physical, emotional domains along with the total VHI scores. Similarly, breathiness also had a

strong positive correlation with all the three domains of VHI. Strain also had a strong positive correlation with the functional domain. Total GRBAS scores also had a strong positive correlation with the

emotional domain and total VHI scores. Very strong correlations were noted between strain and the emotional domain, as well as the total GRBAS score with the physical domain ($P < .05$, $r = .80$ to 1.00).

Table 1: Correlation of the Voice Handicap index (VHI) and GRBAS in patients with pharyngeal cancer pre-treatment and post-treatment

| | | Voice handicap index | | | | | | | | | |
|------|-------|----------------------|---------|------------------------|---------|-------------------------|---------|-------------|---------|----------|---------|
| | | Functional domain | | Physical domain | | Emotional domain | | Total score | | Category | |
| | | r | P value | r | P value | r | P value | r | P value | r | P value |
| Pre | G | .27 | .40 | .07 | .83 | .45 | .14 | .14 | .62 | - | - |
| | R | .77 | .00 | .68 | .02 | 1.00^v | .00 | .68 | .02 | - | - |
| | B | - | - | - | - | - | - | - | - | - | - |
| | A | .10 | .76 | -.15 | .65 | .30 | .34 | -.09 | .79 | - | - |
| | S | - | - | - | - | - | - | - | - | - | - |
| | GRBAS | .40 | .19 | .18 | .57 | .67 | .02 | .20 | .53 | - | - |
| Post | G | .33 | .29 | .71 | .01 | .64 | .03 | .77 | .00 | .63 | .03 |
| | R | .20 | .53 | .79 | .00 | .60 | .04 | .67 | .02 | .37 | .24 |
| | B | .67 | .02 | .66 | .02 | .69 | .01 | .49 | .11 | .35 | .27 |
| | A | .56 | .06 | .44 | .15 | .22 | .49 | .26 | .42 | .12 | .72 |
| | S | .64 | .03 | .77 | .00 | .81^v | .00 | .59 | .04 | .21 | .50 |
| | GRBAS | .44 | .15 | .85^v | .00 | .66 | .02 | .74 | .01 | .48 | .11 |

Note: pre- pre-treatment, post- post-treatment, G-grade, R-roughness, B-breathiness, A-asthenia, S-strain, Category-no complaints to severe voice handicap, r-correlation coefficient, bold represents strong positive correlation.60 to .79 (-.60 to -.79), ^v represents very strong positive correlation.80 to 1.00 (-.80 to -1.00)

Laryngeal Cancer

The correlation of the VHI and GRBAS in patients with laryngeal cancer pre-treatment and post-treatment using Spearman's correlation method is depicted in table 2. Strong and very strong positive correlations between VHI and GRBAS were found before and after treatment ($P < .05$, $r = .60$ to 1.00). Other than strain ($P = .05$, $r = .64$), no other component of GRBAS were strongly correlated with the emotional domain before treatment. All domains of GRBAS were strongly correlated positively with the total VHI score and category. The functional domain was most correlated with the GRBAS domains and total score.

Post-treatment except for the correlation of roughness with the functional domain and asthenia with the total VHI score all domains were strongly positively correlated. Therefore, if the patient perceives voice change (VHI), the clinician also is most likely to detect change in voice quality (GRBAS).

Table 2: Correlation of the Voice Handicap index (VHI) and GRBAS in patients with laryngeal cancer pre-treatment and post-treatment

| | | Voice handicap index | | | | | | | | | |
|------|-------|------------------------|---------|------------------------|---------|------------------------|---------|------------------------|---------|------------------------|---------|
| | | Functional domain | | Physical domain | | Emotional domain | | Total score | | Category | |
| | | r | P value | r | P value | r | P value | r | P value | r | P value |
| Pre | G | .67 | .03 | .59 | .08 | .49 | .16 | .67 | .03 | .72 | .02 |
| | R | .66 | .04 | .58 | .08 | .46 | .18 | .66 | .04 | .72 | .02 |
| | B | .87^v | .00 | .85^v | .00 | .61 | .06 | .82^v | .00 | .88^v | .00 |
| | A | .75 | .00 | .72 | .02 | .51 | .13 | .70 | .02 | .73 | .02 |
| | S | .90^v | .00 | .86^v | .00 | .64 | .05 | .86^v | .00 | .93^v | .00 |
| | GRBAS | .82^v | .00 | .79 | .01 | .55 | .10 | .77 | .01 | .87^v | .00 |
| Post | G | .69 | .03 | .75 | .01 | .86^v | .00 | .79 | .01 | .81^v | .01 |
| | R | .63 | .05 | .66 | .04 | .80^v | .01 | .76 | .01 | .74 | .02 |
| | B | .79 | .01 | .80^v | .01 | .92^v | .00 | .82^v | .01 | .87^v | .00 |
| | A | .64 | .05 | .71 | .02 | .69 | .03 | .60 | .07 | .79 | .01 |
| | S | .67 | .03 | .64 | .02 | .79 | .01 | .74 | .02 | .59 | .00 |
| | GRBAS | .67 | .03 | .74 | .01 | .81^v | .00 | .75 | .01 | .81^v | .01 |

Note: pre- pre-treatment, post- post-treatment, G-grade, R-roughness, B-breathiness, A-asthenia, S-strain, Category-no complaints to severe voice handicap, r-correlation coefficient, bold represents strong positive correlation.60 to .79 (-.60 to -.79), ^v represents very strong positive correlation.80 to 1.00 (-.80 to -1.00)

Difference between Pharyngeal and Laryngeal Cancer

The difference between VHI and GRBAS before and after treatment in both the pharynx and larynx groups using the Mann Whitney U test is depicted in table 3. The mean and standard deviation demonstrate that in the pharynx group voice worsened post-treatment while in the larynx group, voice showed mild improvements. Overall scores show that the larynx group had more voice problems when compared to the pharynx group. All parameters before treatment were statistically different when both groups were compared ($P < .05$). After treatment only roughness, breathiness, asthenia and strain were statistically different ($P < .05$).

Table 3: Difference between the Voice Handicap index (VHI) and GRBAS in patients with pharyngeal and laryngeal cancer pre-treatment and post-treatment

| | TOOLS | Pharynx | Larynx | Statistic value | Probability value |
|--------------|----------------------|----------------------|-------------|-----------------|-------------------|
| | | Mean ± SD | Mean ± SD | Z | P value |
| pre | G | 1.17±.39 | 3.30±1.16 | -3.67 | .00 |
| | R | 1.17±.39 | 3.40±1.08 | -3.74 | .00 |
| | B | 1.00±.00 | 2.80±1.40 | -3.38 | .00 |
| | A | 1.00±.45 | 2.90±1.45 | -2.63 | .01 |
| | S | 1.00±.00 | 2.80±1.40 | -3.38 | .00 |
| | GRBAS | 5.58±1.00 | 15.20±6.16 | -3.44 | .00 |
| | F | 1.33±2.27 | 19.10±14.01 | -3.52 | .00 |
| | P | 3.33±4.23 | 17.90±15.21 | -2.79 | .01 |
| | E | 1.00±2.89 | 17.90±14.29 | -3.49 | .00 |
| | total score | 5.67±8.52 | 54.90±42.83 | -3.31 | .00 |
| VHI category | 1 (1-1) ^a | 2 (1-3) ^a | -3.04 | .00 | |
| | | Mean ± SD | Mean ± SD | Z | P value |
| post | G | 1.75±.87 | 2.50±1.27 | -1.45 | .15 |
| | R | 1.92±.79 | 2.80±1.14 | -1.95 | .051 |
| | B | 1.17±.39 | 2.60±1.35 | -2.76 | .01 |
| | A | 1.33±.49 | 2.50±1.35 | -2.03 | .04 |
| | S | 1.25±.45 | 2.30±1.34 | -2.02 | .04 |
| | GRBAS | 7.42±2.39 | 12.70±6.18 | -1.87 | .06 |
| | F | 5.00±7.43 | 12.40±11.92 | -1.09 | .27 |
| | P | 6.50±9.80 | 11.60±11.15 | -1.43 | .15 |
| | E | 3.50±6.17 | 8.60±10.93 | 1.04 | .30 |
| | Total score | 15.67±22.42 | 32.60±32.74 | -1.42 | .16 |
| VHI category | 1 (1-3) ^a | 1(1-3) ^a | -1.27 | .21 | |

Note: pre- pre-treatment, post- post-treatment, G- grade, R- roughness, B- breathiness, A -asthenia, S- strain, F- functional, P- physical, E- emotional, Category- no complaints to severe voice handicapSD – standard deviation, statistic value (Z), probability value (P), bold signifies statistical significance, ^a- Median (Min-Max)

DISCUSSION

Voice enables people to communicate, and hence its deficit can lead to great morbidity affecting one's personal, professional as well as social life. Voice assessment is of prime importance in head and neck pathologies, as it can be affected by lesions of the pharynx or larynx. These patients can present with symptoms like hoarseness of voice, change in voice character, dysphagia or can also be asymptomatic.

Various tools have been developed for voice assessment which include patient or clinician reported measures and instrumental assessments. These tools help to document the status of voice at any given point of time. Voice status can change over

a period due to effects of treatment, treatment failure or disease progression.

VHI and GRBAS are commonly used tools for voice assessment in head and neck cancer. A proper understanding of the relationships between these two tools in cancers of the pharynx and larynx is important to help clinicians have an overall insight of one tool in relation to another, i.e if one is not performed or missing.

Voice Handicap Index

VHI depicts a patient's perception of the effect of voice change on their physical, functional, and emotional aspects in their life. It demonstrates the impact of voice change on quality of life of the patient. Therefore, it can be used during goal setting

as part of voice rehabilitation. The incremental achievement of these goals acts as positive reinforcement for the patient, improving their confidence and making their social integration easier.

GRBAS

It is a clinician rated voice quality assessment tool. The five parameters such as hoarseness, roughness, breathiness, asthenia and strain provide an insight as to what to look for during visual examination. It helps us monitor the overall severity of these parameters along with the gross fluctuation in a particular parameter.

Correlation of VHI and GRBAS-Pharynx

The correlation between VHI and GRBAS in patients with pharyngeal cancer was not strong. VHI and GRBAS on patients with pharyngeal cancer had shown that these two tools do not correlate strongly in patients with pharyngeal cancer especially before treatment.

In patients with pharyngeal cancer their perception may differ from clinician perception about the severity of their symptom. This difference in perception changes decreases after treatment, mainly because of the effect of treatment or disease progression with time. Hence, we found that there was a trend towards increased correlation between various components of GRBAS with that of VHI after treatment.

Correlation of VHI and GRBAS-Larynx

There exists a significant correlation, across all domains, between VHI and GRBAS amongst the patients of laryngeal cancer both before and after treatment. This result is along the expected lines as larynx is the voice producing apparatus, hence the changes in voice is perceived by patient as well as clinician for these patients. In laryngeal cancer, clinician perception of patient voice problem is similar to what is perceived by patient.

Correlation between VHI and GRBAS

In our study we found a correlation between the subscales of GRBAS and VHI.

This meant that if one parameter was affected there could be an impact on the others in patients with cancers of the larynx. There was positive correlation between VHI and GRBAS in patients with pharyngeal cancer, but it did not reach statistical significance in all domains. Similar findings were observed with VRQOL (voice related quality of life); such as socio-emotional and physical domains. [11] They reported that there was a correspondence between the clinician and the patient's perception, and the patient's perception was poorer. Patients may under-represent or over represent problems for a variety of reasons. Therefore, these tools may be complimentary and not supplementary to each other to provide overall information.

Our study showed strong correlations in the pharynx post-treatment and in the larynx group for both tools. This was similar to the findings of Sabir et al who analysed the same variables in healthy Moroccan students. [12] The current study found strong correlation of roughness in the pharynx while they found strong correlation of breathiness with all subscales of VHI.

If a patient with laryngeal cancer reports any voice change before or after treatment, it should be looked at with high index of suspicion as VHI is significantly correlated with laryngeal cancer. These patients should be evaluated thoroughly. There was positive correlation between VHI scores and GRBAS in pharynx before and after treatment, however these correlations did not reach the level of significance in our study. With sub-factor analysis of GRBAS and VHI there were significant correlation between VHI and roughness before treatment and significant correlation of most parameters of GRBAS. Hence any gross voice change in a patient with pharynx should not be overlooked and should be evaluated.

Implication of this correlation

VHI and GRBAS have different correlation in patients with pharyngeal and laryngeal carcinoma. A laryngeal carcinoma

patient tends to have more severe voice pathology which is equally perceivable by both clinician and patient. However, in pharyngeal pathology the impairment in voice pathology is not as severe and perception of clinician and patient may differ regarding the same.

In cases of laryngeal cancer patient, doing worse on VHI means that he should undergo GRBAS also. Hence any patient with complaint of subjective perception worsening voice with laryngeal cancer should undergo further evaluation.

CONCLUSION

VHI and GRBAS are two common tools used for voice assessment. These tools have significant correlation between them irrespective of treatment in patients with laryngeal cancer. Any laryngeal cancer patient with complaints of worsening voice quality should undergo further evaluation. However, since the correlation was lesser in pharyngeal cancer, any gross change in voice should be evaluated.

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Informed consent was taken from all participants before being enrolled into the study.

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